IN THE SERVICE OF YOUTH

THE second* of two recently published reports concerned with the way in which the State should assist in the service of youth has met with much more sympathetic public response than the first†. The Committee was set up by the Minister of Education just over a year ago, under the chairmanship of the Countess of Albemarle, and has completed its inquiry with exemplary promptness. Invited to "review the contribution which the Youth Service of England and Wales can make in assisting young people to play their part in the life of the community, in the light of changing social and industrial conditions and of current trends in other branches of the education service; and to advise according to what priorities best value can be obtained for the money spent", the Committee quickly realized that it had been convened none too soon and that speedy action would be required if the Youth Service were to flourish. It is not surprising to learn from the Report that the Committee was always aware that it was working against time and that the recommendations made should be regarded as in the nature of a blood transfusion. Side by side with the Committee's proposals for immediate adoption come proposals which would ensure sustained and continued nourishment if the blood transfusion succeeds in restoring the health of a sickly and dispirited child.

The main factor contributing to the sense of urgency which governed the Committee's inquiry is, of course, the 'bulge'. For every five young people between the ages of fifteen and twenty in Britain to-day there will be, in 1964, six young people. Although the increase will not be spread evenly across the country as a whole, all areas and each kind of area will show some increase; in some new towns the increase may be as much as five-fold. Between 1964 and 1970 the total number will decline gradually, but will still remain substantially higher than that of to-day. From 1970 there is again the probability of a gradual increase. The inadequate facilities which are available in the Youth Service to-day are quantitatively insufficient to meet demands which are already upon us. Measures taken to meet the impact of the 'bulge' in the schools and technical colleges and the universities have not been matched with similar provision to prepare the Youth Service for the needs of the increased population. The Committee quickly recognized that unless action is taken at once the 'bulge' generations will leave school only to find a Youth Service inadequate to cope even with its earlier responsibilities.

The effects of the 'bulge' will be reinforced by the cessation of National Service. During the past few years military commitments have kept about 200,000 young men between the ages of eighteen and twenty out of civilian life. Its gradual abandonment during the next two or three years will leave this number of young men available for civilian employment and leisure pursuits. Despite sincere beliefs that National Service has had a wholly unsatisfactory effect upon the lives and characters of many young men in leading to excessive drinking and sexual promiscuity, it is generally accepted that it has provided the majority of those serving with challenge and adventure suitable to their age and needs. The nation, and the young men themselves, will be the poorer unless the Youth Service can provide, in relevant civilian terms, opportunities to match those which come through National Service. The cessation of National Service and the arrival of the 'bulge' will make the Youth Service responsible for about a million more young people in 1964 than it had to cater for in 1958.

A third factor which strengthened the Albemarle Committee's belief that the Youth Service needed immediate support is the unfortunate emergence of a new climate of crime and delinquency. Without wishing to exaggerate the incidence of delinquency, which still involves in any one year only about 2 per cent of boys aged fourteen and less than twenty-one and only 0·2 per cent of girls of the same age group, it is still the fact that, of the total number of persons found guilty of indictable offences in 1957, about 50 per cent were less than twenty-one, and 30 per cent were aged 14–20 inclusive. Whether the figures are large or small in relation to the total population, the crime problem is largely a youth problem, and one in which the public can reasonably expect the Youth Service to play a considerable part in its solution.

To meet the challenge of the 'bulge' and the opportunities provided by the cessation of National Service, as well as to serve the nation in helping to combat the incidence of delinquency among young people, demands a Youth Service made up of virile and enthusiastic men and women dedicated to their calling. This was scarcely the position which confronted the members of the Albemarle Committee during their investigations. Instead, the Committee found leadership suffering from shortage of money and lack of encouragement. Leaders, feeling unsupported and unappreciated, have looked for some sign that their work is nationally recognized as important. They find it neither in official expressions of policy nor in the rewards of a salary scale for those who are full-time which would put the work on a level with cognate professions. They seem to themselves to be in danger of becoming cut off from the march of social and educational advance, and it is neither surprising that the total number of full-time youth leaders is declining nor that full-time posts are failing to attract applicants with the desired qualities.

* Ministry of Education. The Youth Service in England and Wales: Report of the Committee Appointed by the Minister of Education in November, 1958. Pp. iv+136. (Cmnd. 929.) (London: H.M. Stationery Office, 1960.) 6s. net.
† Ministry of Education. 15 to 18: A Report of the Central Advisory Council for Education (England). Vol. 1: Report. Pp. xi+519. (London: H.M. Stationery Office, 1959.) 12s. 6d. See also *Nature*, February 6, p. 341.

For the running down of the Youth Service and the decline in morale of its leadership, the main responsibility must be pinned on the door of the Ministry of Education. The high hopes raised in 1939 by the issue of Circular 1486 by the Board of Education, which was commended (see *Nature*, 146, 627; 1940) as an imaginative act by the Government, have been dashed by subsequent performance. During the ten years up to the end of 1958, the Ministry has not issued a single circular devoted solely to the Youth Service. During the same period there have been ten circulars having some bearing on the Youth Service and seven of them imposed restrictions. The Select Committee on Estimates, in its Report of July 1957, referred to this discouraging effect and put it down to "lack of interest on the part of the Ministry of Education in the present state of the Service and the apathy about its future"*.

In view of the Ministry discouragements, it is not surprising that many local education authorities have shown quixotic attitudes towards the Youth Service. It may seem incredible, but some so-called progressive authorities have no youth committee and no youth officer. Even authorities which value the Service show surprising variations in their practical approaches to its methods of organization and administration and, as a result, there is no accepted minimum standard of services which voluntary bodies of standing can expect from every authority as a matter of course.

It is, indeed, a tribute to the voluntary organizations—and of the voluntary principle which permeates the Youth Service—that the Youth Service has continued to remain in being at all. Apart from the time and devotion given to the Service by so many voluntary helpers—which may include members of local authorities in their official capacities as well as unpaid representatives of voluntary organizations—the taxpayers and ratepayers are usually surprised to learn that the financial weight of the Youth Service falls mainly upon the voluntary organizations. The Standing Conference of National Voluntary Youth Organizations has stated that it is not unusual for its member organizations to have to raise from private and voluntary sources 90 per cent of its total yearly expenditure on headquarters administration, the provision of regional organizers and the training of leaders. Against this, the total sum spent on the Youth Service from the Ministry of Education and local education authority funds in 1957–58 amounted to the not very grand total of £2¾ million; of every pound spent on education, about 1*d*. went to the Youth Service. Where the Ministry can fairly be charged with dereliction of duty is brought home by the Committee's finding that, during the twelve years up to and including 1957–58, direct expenditure by the Ministry on the Youth Service in terms of real money has fallen by a quarter. It is little wonder that many voluntary workers have lost heart and grown weary of working in the dingy, dilapidated buildings with insufficient equipment which have become the trade mark of so many youth clubs.

Much of the Albemarle Report is rightly given to this analysis of why the Youth Service has failed to march with the times; public opinion should see that, in the national interest, central and local government should not again fail in their duty. To give a clear and unequivocal lead, the Committee makes certain minimum recommendations for immediate action which the Government could ill afford to ignore. Sir David Eccles is to be congratulated for accepting this and for the unparalleled action of asking the House of Commons to accept, in principle, all the recommendations in the Report on the day of its publication.

The main proposal is that the Minister should initiate a ten-year development programme, divided into two stages of five years each. During the first five years advances should be made in each sector of the Youth Service to "catch up with a situation already upon us". During the second five-year period the permanent structure should be securely established. Throughout the period of development, the Minister should have at his disposal the best possible advice and help. The Committee wisely recommends the appointment of a Youth Service Development Council which will be little concerned with administration and far more with inquiry, with the sharing of ideas and the promotion of new activities; on occasions, it may serve to rejuvenate a flagging Minister. This Council has, in fact, now been formed and consists of: the Countess of Albemarle (for a period of one year); Mr. Richard Hoggart, a member of the Albemarle Committee and author of "The Uses of Literacy"; Mr. Christopher Brasher, athlete and journalist; Dr. W. Watson, sociologist from the University of Manchester; Miss M. E. Keatley, Staffordshire head mistress; Mr. Edward Lewis, chairman of Decca; Mr. Timothy Raison, journalist; Miss Ellen McCullough, National Woman Officer of the Transport and General Workers' Union; Councillor Alfred Blake, a member of the Portsmouth City Council; Mr. G. S. Bessey, director of education for Cumberland; Miss P. C. Colson, secretary of the Central Council for Physical Recreation; Mrs. Glyn Roberts, former senior mistress in a secondary modern school in Wales; Mr. Huw Wheldon, broadcaster. The Minister of Education himself will be chairman.

As an immediate step, the Report asks the Minister to put in hand arrangements for training 'professional' youth leaders, both for the emergency and the long term. The full-time youth leader force should be increased from the present total of 700 to a provisional one of 1,300 by 1966. To bring this about, an emergency training college should be opened by the autumn of 1961; Sir David Eccles has already indicated that this will be in Leicester. To anticipate legitimate criticisms about the methods of training youth leaders, a working syllabus has been devised which bears close relationship to those used for training teachers. Much here depends upon the choice of the principal, and it is to be hoped that the over-regimentation found in some of the emergency

* Seventh Report from the Select Committee on Estimates. "The Youth Employment Service and Youth Service Grants." (London: H.M. Stationery Office, 1957.)

teachers' training colleges set up after the War may be avoided.

Besides recommendations to ensure that salary scales are commensurate with the responsibilities of the job, and that money is spent in providing building and equipment which give young people who leave school at fifteen or sixteen indoor and outdoor facilities at least equal to those enjoyed by the more privileged who remain in full-time education until they reach years of maturity, the Committee makes two recommendations which deserve close attention.

The first is that the Youth Service should be available for all young people aged 14–20 inclusive. However inadvertent, the proposal to lower the statutory age limit from fifteen to fourteen is a striking comment on one of the fundamental recommendations put forward by the Crowther Committee. This was the unhappy proposal to develop county colleges on a nation-wide scale in about twenty years time. The Albemarle Committee reports how impressed it has been "by the abundance of evidence about the earlier maturity and at least superficial sophistication of many young people in the last school year at the secondary modern school. We know that they are restless and critical then and anxious to move out of the childish world into the freedoms of adolescence. We have been equally impressed by the failure of many children's organizations to hold their members at precisely this age, and by the need all clubs and movements feel to build a bridge between school and life in the world before the boy or girl has actually left school".

No better case for the county colleges has been made out, and the Albemarle Committee is to be complimented for its realistic attitude to the problems of the less intellectually privileged in their last year at school. This minor reform to the Youth Service, however, can in no way be regarded as a substitute for what still remains as the fundamental feature in building a real service of youth. County colleges will not only serve to make earlier transition between school and work and between immaturity and maturity, but will also be the rock around which all the Youth Service should be built.

The second recommendation could easily escape general notice. It is that, during the ten-year period of development, a sub-committee of the local education committee authority (not a sub-committee of a sub-committee) should be charged with responsibility for the Youth Service. The Albemarle Committee recommends that this sub-committee should have the advice of an advisory committee with full representation from voluntary organizations. Now that the Minister has signified his acceptance of the Report, he should see to it that local authorities do not evade their responsibilities for this recommendation. The youth sub-committees should be small and executive in character, and composed of men and women not directly concerned with any youth organizations but enthusiastic about their work. It should not be regarded as yet another committee for politically elected representatives to local councils. To the charge that, with authority to plan and administer the Youth Service, should go responsibility to the electors for public funds should come the reply that the youth committee would be directly responsible to the education committee in recommending expenditure of public monies. If this proposal is adopted, the Albemarle Committee may not only have made a most effective contribution to the establishment of a more virile Youth Service in Britain, but also the beginnings of a reform in local government, which has long been creaking in many joints.

The Countess of Albemarle and her committee are to be warmly praised for the promptitude with which they have discharged their task, and for putting forward a minimum set of practical proposals which the Government would have found difficult not to accept.

CHANCE AND PROVIDENCE

Chance and Providence

God's Action in a World Governed by Scientific Law. By Dr. William G. Pollard. Pp. 190. (London: Faber and Faber, Ltd., 1959.) 16*s*. net.

DR. W. G. POLLARD is the executive director of the Oak Ridge Institute of Nuclear Studies in Tennessee and has also, since 1952, been a priest of the American Episcopal Church. In entering the Christian ministry from an already established career as a physicist, the greatest intellectual problem with which he was faced—a more difficult and decisive question than that of the existence of God—was, as he himself tells us, the problem of reconciling the empirico-causal attitude of science with belief in the providence of God. The present work is the result of eight years of thought about this question.

It soon became clear to Dr. Pollard that it would not do simply to seek for some residual domain of experience which was inaccessible to science and in which divine action might be located. This is the 'God in the gaps' expedient, which has suffered from the successive elimination of more and more of the gaps as scientific discovery has advanced. What he did, however, come to recognize was that the statistical character of scientific law, which has so markedly characterized the modern quantum theory, was in fact really basic even to classical physics, though this was unrecognized owing to the fact that the most tractable, and so the most fully developed, branches of science were those in which this character was scarcely evident. Illuminating examples are given from the realms of fluid dynamics (the problem of turbulent flow), ballistics and the early history of the solar system. (It may be remarked in passing that Dr. Pollard's argument has little in common with the argument by which, in the *British Journal of the Philosophy of Science* for 1950, Dr. K. R. Popper defended a quite different indeterminism in classical physics, an indeterminism which is better described as unpredictability.)

Dr. Pollard then goes on to stress the point that in history, as distinct from science, it is always the individual events that are significant; it is the *facts* that the Egyptians were drowned in the Red Sea and that Washington beat Cornwallis at Yorktown that have radically affected the subsequent course of

the world's history, not the probabilities that those events would happen given the particular circumstances. This point is amplified by a discussion of the difference between scientific time, in which the origin of the time-coordinate is quite arbitrary, and historical time, in which the contrast between the unalterable past and the (as yet) undetermined future is fundamental, though it is also remarked that, with quantum theory, historical time has invaded the domain of science itself. It is also emphasized that miracle, as properly understood, is in no way contradictory to scientific explanation, for it should be thought of not as an interference with or a suspension of scientific law, but as a (scientifically) highly improbable correlation of natural causes, none of which violates any known scientific law: and, as regards allegedly unique events, such as the Creation, the Incarnation and the Resurrection, no question of chance or probability arises, for it is only in the case of events which are in principle indefinitely repeatable that the concept of probability can be applied. The book concludes with a discussion of freedom and providence, in which it is suggested that something similar to, though not identical with, the principle of complementarity in physics may be needed in other fields of science in order to remove the elements of historical time from the systems which are the object of scientific study, and the conception of the twofold nature of reality is further illustrated by the use of Dr. Martin Buber's distinction between 'I-it' and 'I-thou' relationships.

This is an important, if not entirely an easy book, and it is particularly to be commended for its author's thorough grasp of both the realms with which he is concerned—those of science and of theology—and not, as so often is the case in books on this subject, with only one of them, and for his determination to think the problems through to the end and not to be content with superficial or makeshift solutions.

E. L. Mascall

RADIOISOTOPES IN MEDICAL AND BIOLOGICAL RESEARCH

Radioisotopes in Scientific Research

Proceedings of the International Conference held in Paris in September 1957, under the auspices of the United Nations Educational, Scientific and Cultural Organization. Edited by Prof. R. C. Extermann. Vol. 3: Research with Radioisotopes in Human and Animal Biology and Medicine. Pp. xxi+763. Vol. 4: Research with Radioisotopes in Plant Biology and some General Problems. Pp. xxi+690. (London and New York: Pergamon Press, 1958.) 140*s.* net each.

ON looking through the voluminous publication on "Research with Radioisotopes in Plant Biology" (Vol. 4) and in "Human and Animal Biology and Medicine" (Vol. 3), one could argue whether it is useful to compile so much heterogeneous material from diverse fields of biology, only because the same technique is applied.

However, when reading the two volumes under discussion, these doubts are dispelled, for in the case of research with isotopes the common tie is not only a special technique but also a typical point of view. We might call this a new kind of dynamic biology, which only began with the introduction of the tracer techniques, and the results of which have nowhere been laid down more impressively than in these collective volumes.

The dynamic state of certain constituents of organisms is continuously being subjected to a kinetic analysis, regardless whether one examines the transport of electrolytes through the cell membrane and other general permeability phenomena, the effect of fertilizers, the synthesis of protein and nucleic acid, raw products of plants such as rubber, or the turnover of the most vital constituents of the healthy or pathological organism. The study of work in fields unfamiliar to the reader therefore acts as a stimulus for new ideas and the devising of new techniques in his own work.

Vol. 4, which is devoted to "Plant Biology and some General Problems", also comprises a series of specialized work in the field of animal physiology, so that zoologists and medical men for this reason should consult also both volumes.

It is very commendable that several papers are produced with many more useful details than were contained in the original lectures, and that techniques in particular are discussed at great length and many useful illustrations are added.

Otto Hug

PETROLEUM GEOLOGY

Geochemical Methods of Prospecting and Exploration for Petroleum and Natural Gas.

By A. A. Kartsev, Z. A. Tabasaranskii, M. I. Subbota and G. A. Mogilevskii. English translation edited by Paul A. Witherspoon and William D. Romey. Pp. xxiii+349. (Berkeley and Los Angeles: University of California Press; London: Cambridge University Press, 1959.) 94*s.* net.

THIS book presents a comprehensive survey of the geochemical methods of petroleum and natural gas prospecting and exploration being used in the U.S.S.R. in 1954 and reflects the large scale of the Russian effort in this field. The authors in a preface state that the changes which have taken place between publication of the Russian and American editions are mainly a matter of emphasis. However, it is probable that some of the analytical techniques have by now been modified or superseded and that methods which are briefly mentioned as being developed are now established techniques.

The standard of the translation is high but the lack of exact English equivalents for some of the Russian technical terms and the differences in Russian and English syntax has, on occasion, caused some difficulties. There are more typographical errors than should be expected in a technical book of this character, and the maps and figures, as in so many Russian publications, are often far from clear. In particular, no scales are given for the maps.

The first three chapters deal with the basic concept underlying the subject and include a more than adequate description of the geochemistry of oil formations and of gases. The remaining chapters consider geochemical methods which have proved to have a definite practical application. These include gas and core gas surveys, oil and gas logging, bitumen, bitumen luminescence, hydrochemical, radioactive, soil salt, oxidation reduction potential and microbiological methods. Various other methods which

have been mentioned in the Russian literature, but which were not adjudged by a conference on geochemical methods of prospecting for petroleum and natural gas (Neftyanoye Khozyaistvo, 1955) to be of proved usefulness, are not considered.

Each method is described in the logical order of theoretical basis, field procedure, analytical techniques and interpretation of results. The equipment for various alternative sampling and analytical techniques is described in detail. Although, in general, more comment on the relative merits of the methods and techniques would have been appreciated, the authors do not hesitate to criticize those methods, whether Russian or American, with which they do not agree on theoretical grounds.

Mention is made on a number of occasions of the difficulties of distinguishing true anomalies from false anomalies resulting from biological activity and other causes. The interpretation of leakage dispersion patterns is dependent on a considerable number of variables, yet this aspect of the subject is only relatively briefly discussed. The inclusion of additional case histories presenting all the data, their interpretation and the results of subsequent drilling would have been of great interest.

The authors consistently emphasize the necessity for correlating the data from different types of geochemical methods and the results of these methods with geophysical and geological information. Geochemical methods of prospecting and exploration are not a universal panacea but are additional tools in the hands of the geologist. The geochemical prospecting methods described in this book are considered to have proved their worth under certain conditions but, as with all methods of prospecting, their application is limited to those areas where conditions are favourable.

Despite some few shortcomings, this book gives a well-balanced picture of the application of geochemical techniques and is recommended to petroleum geologists interested in obtaining a knowledge of these new and rapidly developing methods, which may give valuable additional information in the search for oil deposits.

JOHN S. TOOMS

GROWTH OF PRIMARY EDUCATION

Primary Education

Suggestions for the Consideration of Teachers and Others concerned with the Work of Primary Schools. Pp. xiii+334. (London: H.M. Stationery Office, 1959.) 10*s*. net.

THE development of efficient methods of teaching in primary schools, improved organization of the schools themselves, and a markedly greater degree of achievement by the children have resulted from a widespread and quickening interest in primary work by teachers and the general public. This is well brought out in this Ministry of Education publication, which shows that the rise in children's achievements has not come about suddenly or by mechanical application of any special methods or practice, but because teachers, from their experience and from the growing body of research available to them, have come to understand better the ways in which children learn, and have applied their knowledge to good purpose.

The book is in effect an anthology of the ideas and practices which present-day teachers are successfully developing in the schools.

Twenty years ago junior schools were only tentatively striking out towards what is now common practice. Less than half the children between eight and twelve years of age were in schools separate from those containing older children also. Now, more than nine-tenths of school children up to eleven years of age are in separate infants schools, separate junior schools, or schools for children between five and eleven only.

'Primary Education' calls for a more critical consideration by teachers of the quality and substance of what is offered to the children for their learning, and for a firmer realization that children's capacities, whether small or great, should be exercised to the full.

For the man of science, one of the most interesting sections is that concerned with the teaching of mathematics. There is little doubt that deficiencies in the primary school must bear considerable responsibility for subsequent failures in mathematics. Teachers in primary schools can do much to prevent the positive dislike of mathematics which is so common in older children. It is to be hoped that the new three-year training college courses will produce primary school teachers who can get away from teaching mathematics by rote and will be able to teach young children in a meaningful way.

CONURBATIONS OF GREAT BRITAIN

The Conurbations of Great Britain

By T. W. Freeman. With a chapter on the Scottish Conurbations by Catherine P. Snodgrass. Pp. xii+393 (66 maps). (Manchester: The University Press, 1959.) 37*s*. 6*d*. net.

PATRICK GEDDES' term 'conurbation', more narrowly defined by Fawcett, is a vitally important but vague geographical concept that calls for searching analysis of criteria and their cartographic representation. For this reason we turn to this book with special interest.

As to content, Chaps. 1 and 12 should be read first. Then those of the intervening chapters about the conurbations (or the ensemble of minor conurbations) of most interest should be read. For the book is heavy in topographical detail that becomes irksome in spite of the aid of maps. The sectional treatment of each conurbation includes physical features, historical growth, distribution and movements of population, and, a main feature, the growth of the patterns of administrative areas. The work depends on geographical and historical studies as well as on the interesting data contained in reports of past commissioners and the census reports. It contains 66 maps, 25 of which show the changing patterns of the administrative areas in each conurbation.

Freeman, following Fawcett, has attempted to define every conurbation by the extent of its built-up area. There are seven major conurbations, each of which receives a separate chapter in the book. Fourteen minor conurbations have 250,000–750,000 inhabitants. These include several 'clusters' of

special interest—the South Wales valleys, Sheffield–Rotherham (Geddes' South Riding), the Lancashire Coalfield (Wigan–St. Helens), and the Potteries. Some of these areas already form more extensive and almost contiguous clusters, as envisaged by Geddes. The whole South Wales area (Geddes' Walestón) has 1·1 million people. Nottingham and Derby are also linked with 850,000. The Sheffield and Barnsley areas are virtually one. Manchester and Liverpool are interconnected through the Lancashire coalfield area (Geddes' Lancaston). The smaller conurbations (50,000–250,000), 75 in number, are treated in two chapters. Portrayals are necessarily brief and encyclopædic.

This book is essentially a descriptive compilation. This is how Freeman chose to write it; but the approach will not advance geography as a research discipline or as a contributor to planning. He does not formulate and systematically develop any geographical concepts with regard to urban growth, an approach that would necessitate a complete reorganization of the book, but would yield more worth-while results. Geographers need to concentrate on particular problems in the spatial structure of our urban society, some of which are sandwiched in the pages of this book. Here are involved questions of criteria, cartographic analysis, and interpretation that cry out for investigation, and are especially fitted to the expertize of the geographer. The defects of this book point to this need, and it is to be hoped that Freeman and his colleagues will apply themselves to it.

R. E. Dickinson

STUDIES IN RHEOLOGY

Transactions of the Society of Rheology

Vol. 2. Edited by R. D. Andrews. Pp. ii+314. (New York: Interscience Publishers, Inc.; London: Interscience Publishers, Ltd., 1959.) 64*s*.

Rheology of Disperse Systems

Proceedings of a Conference organized by the British Society of Rheology, and held at the University College of Swansea, September 1957. Edited by C. C. Mill. Pp. vii + 223. (London and New York: Pergamon Press, 1959.) 60*s*. net.

THE "Transactions of the Society of Rheology" constitute the proceedings of the annual conferences of the American Society. In 1957, the conference was held in the Textile Research Institute, Princeton, New Jersey. The second of these volumes contains sixteen complete papers and a number of abstracts.

The organizers are to be congratulated on the excellent balance of the programme. It would be tempting to give a heavy preponderance to papers dealing with work in the one or two industries which now employ a high proportion of rheologists; but this has not been done. Theory and practice over a wide field are discussed.

In an introductory paper, A. S. Nowick outlines the career of C. M. Zener, who received the Bingham Medal. Dr. Zener is distinguished in other fields, and it is estimated that his rheological work constitutes less than half his scientific output.

On the more academic side, the subjects treated include work on viscosity–concentration relations in suspensions, relaxation spectra distributions of high polymers, equations for the interconversion of relaxation and retardation spectra and a general study of capillary viscometry.

Papers on applied rheology range over a wide field: the peeling of adhesive tapes, liquid flow in roll nips, creep of snow, mechanical breakdown of bundles of fibres and a fair number of articles on high polymers.

The paper by A. B. Metzner and M. Whitlock is worthy of special mention. Since Osborne Reynolds published his classical work, it has been well known that certain pastes and suspensions become firmer on shearing. All such phenomena have tended to be classed as 'dilatancy', it being assumed that closely packed particles must first pass into open packing before the system can flow, thus producing an increase in volume. This paper confirms what has long been suspected, that the increase in consistency is not necessarily associated with dilatancy at all and often happens at concentrations not corresponding to close packing. The true explanation remains an outstanding problem for rheologists.

The 'Transactions' will certainly provide an excellent annual survey of the progress of rheology in the United States. It is a pity only that this particular volume has taken so long to appear.

It is difficult to review a collection of eleven papers which, though they are all concerned with dispersed systems (must one omit the grammatically required 's' ?), cover so wide a range of subjects and materials. Yet it is fair to say that, though the standard of the articles differs considerably, the general level is remarkably high.

Prof. J. G. Oldroyd's presidential address deals with the mathematics of 'complicated rheological properties', because, as he points out, simple properties are of little interest to the mathematician. This is fortunate, in view of the complexity of the materials generally studied by practical rheologists.

S. G. Mason and W. Bartok contribute a paper of considerable theoretical interest on the hydrodynamics of suspensions and emulsions, and R. L. Whitmore gives some reasons why, on theoretical grounds, suspensions flowing through capillaries fail to obey Poiseuille's fourth-power law, applying his theory to the very important problems of the flow of blood. Since this paper was read, it has stimulated considerable further work. Also N. Casson's and E. Bantoft's contributions, in which they propose a very simple but hitherto unused equation to relate shear stress to rate of shear, has been followed by the publication of descriptions of a number of applications to materials other than varnishes and inks, including blood and molten chocolate. The latter forms the subject of an article by E. H. Steiner, but it was after the conference that he discovered the usefulness of Casson's equation for this material.

A. Jobling and J. E. Roberts, using Weissenberg's deformable membrane technique, describe complex dilatancy effects in certain suspensions which still elude any mechanical explanation and yield a strong incentive to further study. Other papers deal with high polymers, adhesive sealing compositions ('lutings'), starch-clay mixtures and gaseous fluidized beds. This is clearly a conference which immediately activated further research, thus fulfilling the prime purpose of all such gatherings.

The publishers are to be congratulated on the excellent production of the book. A welcome appendix gives the addresses of all authors and contributors to the discussions.

G. W. Scott Blair

TERCENTENARY CELEBRATIONS OF THE ROYAL SOCIETY

THE programme of events which are to comprise the tercentenary celebrations of the Royal Society, due to take place during July 18–26, indicates that not only is the historical importance of the event to be appropriately marked but also that those who are to take part will have a good opportunity to become acquainted with active research work now being carried out in Great Britain.

Formal participation in the full programme will be limited to Fellows and Foreign Members of the Society and to those already invited to represent at the celebrations national academies of science, selected universities throughout the world, and appropriate international scientific organizations. The majority of the Foreign Members of the Society have already notified their intention of being present, and other distinguished men of science are among those who are coming from some fifty different countries. The British Commonwealth will be particularly well represented by large numbers, many of whom are Fellows of the Royal Society. The presence in London of so many leading scientists promises to make the occasion an outstanding scientific event.

In addition to the formal participants and their accompanying relatives, for whom the full programme of events has been principally devised, there will be a number of events to which others will be invited, notably the formal opening ceremony on the afternoon of July 19, which is to take place in the Royal Albert Hall. The ceremony will take the form of a few short speeches and the presentation of formal congratulatory messages by selected representatives attending the celebrations. For the occasion, Sir Arthur Bliss, Master of the Queen's Musick, is composing a "Salute to the Royal Society", and this will be played by Dr. G. Thalben-Ball on the organ together with the trumpeters and other musicians from the Royal Military School of Music, Kneller Hall. After an interval for tea the Society's president, Sir Cyril Hinshelwood, will deliver the tercentenary address.

In honour of the occasion the Universities of Oxford, Cambridge and London will have special honorary degree ceremonies, when degrees will be conferred on distinguished scientists attending the celebrations.

The Oxford and Cambridge ceremonies will take place on July 21 and July 25, respectively, during visits to these Universities. While in Oxford, visits will be paid to the Colleges which will receive the Royal Society visitors at lunch. The conferment of honorary degrees will take place in the Sheldonian Theatre, the architect of which was Sir Christopher Wren, former president of the Royal Society, and this will be followed by a garden party at Wadham College, where meetings of importance in relation to the foundation of the Society took place. John Wilkins, Bishop of Chester and Warden of Wadham, was one of the Society's first secretaries. The visit to Cambridge will have a similar pattern, and in both Universities special exhibits relating to former Fellows of the Society are being specially arranged.

The University of London ceremony will take place in the Royal Festival Hall on July 22, where H.M. Queen Elizabeth the Queen Mother as Chancellor of the University will confer honorary degrees.

The following lectures will be delivered during the period of the celebrations in the Royal Institution, the Royal College of Surgeons, and the Beveridge Hall of the University of London: "Genetics and the Structure of Biology", by Prof. C. D. Darlington; "Trends in Aeronautical Science and Engineering", by Sir Arnold Hall; "The Evolution of Nuclear Power Plant Design", by Sir Christopher Hinton; "The Physics and Chemistry of Nervous Conduction", by Prof. A. L. Hodgkin; "Molecules in Crystals", by Dr. Dorothy Hodgkin; "The Investigation of the Universe by Radio Astronomy", by Prof. A. C. B. Lovell; "The Problems of Transplantation", by Prof. P. B. Medawar; "The Study of Nuclear Interactions at Very Great Energies", by Prof. C. F. Powell; "New Horizons in Organic Chemistry", by Sir Alexander Todd; "The Metamorphosis of Insects", by Prof. V. B. Wigglesworth.

The programme includes visits to university, government and industrial research laboratories which are or have been associated with the work of Fellows of the Society. In addition to visits to the Universities of Oxford and Cambridge, there are formally organized visits to the Imperial College of Science and Technology and University College in London, as well as informal visits privately arranged. The National Physical Laboratory, the Royal Botanic Gardens, Kew, the National Institutes for Medical Research, for Research in Nuclear Science and for Research in Dairying, as well as the Royal Aircraft Establishment, the Atomic Energy Research Establishment, the Geological Survey and Museum, and the Radio Research Station and Road Research Laboratory (Department of Scientific and Industrial Research) are among the national research institutions to be visited. The British Museum (Natural History) and the Science Museum are arranging special visits. The Associated Electrical Industries, Ltd., Research Laboratory at Aldermaston, the British Petroleum Research Centre, the General Electric Co. Research Laboratories, the Glaxo Research Laboratories, Imperial Chemical Industries, Ltd. (Plastics Division), the Wellcome Research Laboratories, and several research association laboratories provide a quota of industrial research visits.

Other events or visits recall the historical associations of the Society. The foundation of the Society in Gresham College near Guildhall in the City of London will be commemorated not only by two City receptions, one by the Lord Mayor in Guildhall and the other by the twelve great City Companies in the Mercers' Hall, but also on Sunday, July 24, by a sermon relating to Sir Christopher Wren, to be preached in St. Paul's Cathedral, of which he was the architect. One of the tours will re-visit the present-day Gresham College and also the other former homes of the Society in Crane Court off Fleet Street and Somerset House. Visits to Greenwich, where King Charles II instituted the Royal Greenwich Observa-

tory, and the Chelsea Royal Hospital, built by Wren on a site once briefly owned by the Royal Society, are direct links with the Society's Royal founder. The Royal Mint, where Newton presided as master for many years, and Newton's birthplace at Woolsthorpe are also included in the places to be visited.

The Shell International Petroleum Company is making a special film for the occasion. This will be shown in the Royal Festival Hall on July 22, in a programme which will also include reference to the value of the film as a tool in scientific research. At the Society's tercentenary conversazione, to be held in Burlington House on July 23, a series of exhibits giving a presentation of current research work will be included in the programme of the evening, during which there will also be on display the congratulatory addresses received by the Society on the occasion of its three hundredth birthday. Some of the Society's treasures, such as the original reflecting telescope made by Sir Isaac Newton, the manuscript of Newton's "Principia", the Society's Mace and the Charter Book, both of which are gifts from the Society's Royal founder, will also be displayed on this occasion.

The celebrations will conclude with the tercentenary banquet on July 26, when the toast of "The Royal Society" will be proposed by the Prime Minister.

The issue of the first volumes of "The Correspondence of Isaac Newton", edited by Prof. H. W. Turnbull, happily coincides with the tercentenary year of the Society as a tribute to the Society's greatest Fellow. Two further historical works are being specially issued to mark the tercentenary occasion. These are a new brief history of the Society by Prof. E. N. da C. Andrade, and a volume of the Society's *Notes and Records* which is edited by Sir Harold Hartley. This special volume will give an account of the founder Fellows including Robert Boyle, Christopher Wren, Sir Robert Moray, Viscount Brouncker, Robert Hooke and others, as well as articles on the origins of the Society.

D. C. Martin

SOME CONSEQUENCES OF EXPANSION OF THE EARTH

By Prof. J. TUZO WILSON
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In 1937 Dirac[1] suggested that the gravitational constant G is decreasing with time, proportionally to t^{-1}, where t is the age of the universe. At that time t was considered from astronomical evidence to be about 2×10^9 years, although age determinations indicated a greater age.

In two recent papers Dicke[2,3] has discussed some of the consequences of this hypothesis using more recent estimates for t of $6{\cdot}5 \times 10^9$ and 12×10^9 years, respectively. Using the first figure he concludes that in the past $3{\cdot}25 \times 10^9$ years the circumference of the Earth would have increased by about 4·5 per cent or 1,100 miles at an average rate of about 0·5 mm. a year. He suggests that this expansion should still be recorded in cracks widely distributed over the ocean floors. He also finds no compelling evidence of a physical nature for or against Dirac's hypothesis and speculates whether "the history of the solar system as seen through the eyes of astronomers and geologists may enable fundamental conclusions to be drawn regarding physical interactions in the past". Egyed[4] is another who has long advocated an expansion of the Earth on geological grounds and has estimated a rate of increase in circumference of 3·8 mm. a year.

It is proposed here to examine the geological and geophysical evidence briefly in the light of recent observations.

The information about the Earth has been chiefly contributed by stratigraphers, Precambrian geologists, students of physics of the Earth and oceanographers studying the sea-floor. Unfortunately, it has never been well integrated.

As a result of the International Geophysical Year, progress in oceanography has recently been very rapid. In 1956 Ewing and Heezen[5] suggested that the mid-ocean ridges form a continuous, seismically active belt, extending through the Atlantic, Indian and South Pacific Oceans. They[6] have since stated that a median rift valley already noticed by Hill[7] is a characteristic feature, that it may be the locus of the earthquake foci, and that it (and perhaps the ridge in general) have intense magnetic anomalies "due to a subsurface body of high magnetic susceptibility". A branch of this rift has been traced to the Gulf of Aden[8] and thence to the rift valleys of Africa[9], which have similar geophysical features.

Heezen[10] suggests that the African rifts represent the start of another ocean and that existing ocean basins may have grown by the widening of such rifts under tension, "if, as the Earth's exterior expanded, the continental crust maintained a relatively constant area". Since the oceans occupy more than two-thirds of the Earth's surface, such an expansion would involve nearly doubling the Earth's radius during geological time. The impossibility of this has been pointed out by Teller[11] and is appreciated by Heezen, who mentions that the postulate of an expanding Earth "may have other more serious objection of an astronomical nature".

If, on the other hand, one postulates that only the mid-ocean ridges and not the whole ocean basins have grown, the expansion would have been much less. Their width varies and is not accurately known, but Heezen's estimates seem to range from 400 to 800 miles. The length of the active ridges is 40,000 miles; but echo-soundings by U.S. Submarine *Nautilus* suggest a continuation of the mid-Atlantic ridge across the Arctic basin, parallel with the Lomonosov ridge[12], and it has been suggested that some mid-Pacific ridges form part of the system, although seismically quiescent at present[13,14]. Including these gives a minimum length of the ridges of 60,000 miles and a minimum superficial expansion of about $2{\cdot}4 \times 10^7$ square miles. This would require an increase in the Earth's circumference of about 6 per cent, and the formation of the ridges has probably required all geological time because there are no important abandoned ridges or any obvious way of

disguising them. This is close to Dicke's estimate. This does not prove that expansion of the Earth has occurred or if it has that it is due to change in G, but it is worth considering some of the consequences of accepting that hypothesis.

Bullard[15], who devised a method of measuring heat flow through the ocean floor, and Von Herzen[16] have remarked that over most parts of the ocean floor the flow of heat is equal to that on continents but that it is higher over the mid-ocean ridges. This would be explained if horizontal separation of the original crust along the ridges continually exposed hotter interior layers. This high heat-flow and the absence of any earthquakes of focal depth greater than 70 km. along the ridges suggest that the Earth is only brittle to stresses of short duration to a depth of 70 km. beneath the ridges.

The lower temperature gradients and the occurrence of earthquakes at depths of up to 700 km. under other parts of ocean floors and continents suggest that those parts may be brittle to 700 km.

The alternative explanation that rising convection currents cause the high heat flows is as satisfactory for the mid-ocean ridges, but it has never been shown how sinking currents could account for the very varying types of coasts of different oceans or the patterns of mountain belts. Reduced heat flows found in some trenches could be due to recent flow into them of cold turbidity currents and submarine oozes.

Since the distance to the zone of flow under the mid-ocean ridges may be only one-tenth as much as it is elsewhere, we might expect a rift once formed to remain the site of further expansion.

Opening of rifts along the mid-ocean ridges would tend to make the rest of the Earth's surface buckle at a distance from them. That is where the continents with their mountain system are found. There the increase in radius of curvature would produce local compression above a level of no strain (or neutral surface) along with tension below it. A similar general situation was postulated by Jeffreys[17] as a result of contraction in the Earth, and it was used by Scheidegger[18,19] and Wilson[14,20] to explain the details of mountains, island arcs, grabens and other features. Their explanations are still applicable in principle to the new hypothesis. At the same time, since the brittle shells on the Earth's surface are spherical not cylindrical, the buckling which is considered to produce mountain building would shift in direction as well as in position from time to time. It is conceivable that this change every few hundred million years might be as large as a right angle (for example, from Ural or Appalachian directions to Himalayan or Cordilleran directions), while minor adjustments and seismicity might be expected everywhere.

The view that continents are zoned and have grown during geological time over parts of the former ocean floors[14,21] is compatible with this hypothesis. Indeed expansion removes a major obstacle to this theory. If continents had grown on a shrinking Earth, the oceans would have flooded the continents, and this has not happened.

Recent work[22] on the isotopic ratio of lead ores having volcanic associations also supports the view that they (and hence by analogy other volcanic rocks) have not been reworked but are being emplaced directly from the mantle. This supports the opinion that continents are growing and not being reworked.

The observation that continents are spaced as far from mid-ocean ridges as possible and that there is some parallelism between their margins could be a consequence of the conditions necessary to produce buckling.

The view that continents have drifted apart is supported to a small degree but not to the extent desired by some advocates of continental drift and some students of palæomagnetism. Nevertheless, expansion along the ridges would alter the Earth's principal moments of inertia and could thus induce polar wandering.

One of the chief arguments used in support of convection currents has been that they might explain the rapid horizontal motions observed along large faults such as the San Andreas in California, and the horizontal first motion observed in circum-Pacific earthquakes, although the manner in which they could do this has not been explained. But such motions are also a consequence of the present hypothesis. An active mid-ocean ridge extends across the South Pacific Ocean from the vicinity of New Zealand to South America, where it terminates in two or three branches against the Andes. If this ridge is widening at the rate of about 0·5 mm. a year and if along the Andes and Cordillera there is an existing line of fracture due to buckling, then a northward shearing motion of the Pacific Ocean relative to the Americas could take place along the mountains north of the ridge. Such a northward motion of the Pacific has long been postulated, and the rate is perhaps compatible with the rather uncertain geological evidence[23].

That this shear motion would not occur south of Chile may perhaps explain the absence of any equivalent to the Isthmus of Panama across Drake Passage. Similar motions in the past could account for other shifts, such as those along the Great Glen fault[24] or the Murray scarp[25].

Isostatic balance would certainly be effective in the model Earth proposed, but adjustment would be more readily achieved for the Earth as a whole and for sea-mounts over mid-ocean ridges than elsewhere. This appears to be supported by observations. The suggestions from studies of Earth satellites that the Earth is somewhat pear-shaped[26] might result from the wider distribution of mid-ocean ridges in the southern hemisphere; but it appears to be more easily explained by the recent removal of ice-sheets. Contrary to previous opinion, Sacks and Strelkov[27] report that large ice sheets covered much of northern Siberia during the Pleistocene. Thus the geoid is still much depressed in a zone centred along latitude 60° N., and G. Pratt[28] has reported depression over Antarctica. This would produce a pear-shape without implying great strength over periods of long duration.

It is perhaps worth noting that to a first approximation the mid-ocean ridges lie in the shape of a reversed J folded about the Earth, the stem being in the Atlantic and hook being in the Southern Ocean. Two branches extend northward into the Indian and Pacific Oceans. Also to a first approximation the continents lie in a similar but complementary pattern of a J inverted and folded about the Earth with the stem through Antarctica and the Americas and the hook through Eurasia. Two branches extend southwards into Africa and Australia.

Perhaps this was the initial fracture pattern of the Earth; but the two parts have developed differently. Whereas the mid-ocean ridges have parted without migrating and have emitted basalts, the continental fractures have buckled without parting and have migrated, moving outwards about their nuclei which

seem to preserve evidence of a different, more volcanic and perhaps hotter history of the Earth during a period 2,000–3,000 million years ago[20,21]. It is only the average position of the continental system that at all resembles a *J* for to-day the active fractures have the shape of a *T*, folded about the Earth with its junction in Indonesia, but there are links between the two systems, for example, between Gibraltar and the Azores, between New Zealand and the ridge to the south and in the scarps from California to Hawaii. The volcanoes of the continental system emit more acid lavas than basalts.

Thus the foregoing hypothesis has the merit of appearing to explain many features of the Earth's surface, though this does not constitute a proof. Even if true, expansion at the rate here postulated could conceivably be due to phase changes[22] in the Earth's interior or perhaps to differentiation[23] of the core and mantle, but a decrease in *G* remains an inviting idea. If so a number of geophysical effects discussed by Dicke must be taken into account in calculations about the Earth's interior and these might include secondary effects due to phase changes.

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EXPERIMENTAL TRANSFORMATION OF CELLS*

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THE term 'transformation' will be used rather loosely to cover a wide range of changes produced by various experimental conditions in the structure and functional activities of cells; merely toxic effects leading to degeneration have been excluded. Most of the examples presented have been chosen from experiments on tissues and cells grown in culture, because I myself am familiar with this field.

Part of the work to be described relates to the normal differentiation of tissues, and has been included because it sheds light on some of the morphogenic principles that are concerned in certain types of cellular transformation.

Tissue Interaction

It is now known that the different types of cells of which an organ is composed may exert a profound influence on one another's structure and physiology, especially in embryonic life.

In Spemann's classical experiments on induction it was shown that in early newt embryos certain tissues act as organizers in embryonic development and induce and direct the differentiation of neighbouring structures. That this phenomenon of induction also occurs in warm-blooded animals was first demonstrated by Prof. C. H. Waddington[1] in early chick embryos explanted in culture.

* Substance of a Special University Lecture delivered in the Anatomy Department, Middlesex Hospital, London, on February 2.
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Induction is not restricted to the initial stages of development; an interesting example of its operation at a later stage of embryonic life is provided by the elegant experiments on the formation of feather rudiments, recently published by Dr. P. Sengel[2] from Prof. Etienne Wolff's laboratory. The object of this work was to investigate the interaction of the dermis and epidermis during the development of the feather papillæ. First, Sengel cultivated dorsal skin from chick embryos of 6–6½ days incubation on a very simple medium; he found that under these conditions feather germs would not develop in an explant in which no feather germs had yet appeared (stage 0) unless it were associated with another tissue—neural tube, muscle, etc.; but feather rudiments formed readily in slightly older (stage 1 and stage 2) skin explants. He concluded that at stage 0, feathers would not develop in the absence of certain non-specific external factors which were unnecessary at a later stage. Next, Sengel separated the epidermis from the dermis by Moscona's method of mild tryptic digestion, and then combined stage 0 epidermis with stage 1 dermis: feather papillæ formed in the double explants. No feathers appeared, however, when stage 0 epidermis was associated with slightly older, stage 2 dermis. From this it was concluded that at stage 1 the dermis can induce feather-formation, but that by stage 2 it has lost this inductive capacity. Sengel then combined stage 2 epidermis with stage 0 dermis: feather germs developed; this result showed that

by stage 2 the epidermis had acquired the power to induce the early (stage 0) dermis to form feather papillæ.

These results are a nice example of the reciprocal influence of mesoderm and epithelium during normal development. When isolated epithelium is associated with the wrong mesoderm, however, its differentiation may be profoundly disturbed. Thus Sengel[3] found that when the dorsal epidermis from a stage 1 (6-day) embryo was associated with the tarso–metatarsal dermis of a 12-day embryo, scales developed and the grafted epidermis became transformed into the thick, precociously keratinized epithelium normally characteristic of the shank region.

My former colleague, Dr. C. B. McLoughlin (unpublished work), investigated the influence of mesenchyme from different organs on the differentiation in culture of epidermis isolated by tryptic digestion from the limb-buds of 5-day chick embryos. In control experiments isolated epidermis when combined with limb-bud mesoderm formed an islet of keratinizing squamous epithelium, but when associated with the mesoderm of the gizzard, it failed to keratinize and formed a cuboidal epithelium which sometimes contained ciliated cells and even secreted a little mucin. When enclosed by heart muscle, the epidermis again failed to keratinize and formed a cyst of extremely flattened cells.

The interaction of epithelium and connective tissue in more complex organs has been studied by Grobstein. One set of experiments concerned the submandibular gland rudiment of 13-day mouse embryos[3]. Grobstein separated the epithelial component of the gland from the mesodermal rudiment of its capsule. He found that when the isolated epithelium alone was explanted, it grew as an undifferentiated sheet of cells; when combined with mesoderm from other parts of the body it formed an inactive, rounded mass; but when re-combined with its own capsular mesoderm it formed a branching, glandular tree. Grobstein obtained exactly the same results when he interposed a porous filter between the epithelium and the mesenchyme, although the pores of the filter were too small to allow cells to pass through. From this it was clear that the glandular epithelium requires substances produced by its own capsular cells to allow it to differentiate normally, but that direct contact with the mesenchyme is not essential.

Chemical Influences

This brings us to the subject of transformations induced experimentally by chemical means.

The best known and most widely investigated example of a chemical compound that drastically affects differentiation is vitamin A. In A-deficient animals, many mucous and glandular epithelia acquire a squamous, keratinizing structure very similar to that of the normal epidermis. A similar histological change (unpublished) was recently produced by my colleague, Dr. I. Lasnitzki, who found that when the prostate glands of young mice were grown for 10 days in a protein-free, chemically defined medium containing neither vitamins nor hormones, they developed large areas of heavily keratinized, squamous epithelium which was often continuous with apparently normal secretory epithelium. It is possible, but not yet certain, that this change may be due to the absence of vitamin A in the culture medium.

The late Sir Edward Mellanby and I found that the reverse effect to that of A-deficiency could be produced by growing embryonic chicken skin in a medium containing excess vitamin A (ref. 4). In normal medium the epithelium develops into a squamous, keratinizing epidermis, but in the presence of excess vitamin A it is changed into a mucus-secreting epithelium which is sometimes ciliated.

Dr. McLoughlin (unpublished work) has shown that this response of the epidermis to vitamin A is due to a direct action on the epithelium and is not mediated by the dermis. Pure cultures of epidermis isolated from 5-day chick embryos became keratinized in normal medium, but in the presence of vitamin A it failed to become keratinized and secreted some mucin.

Dr. Stephen Pelc and I[5] investigated some of the early histochemical changes that accompany this mucous transformation, by studying the uptake of various labelled compounds by means of autoradiography. We found that of the amino-acids, leucine and methionine were taken up equally well by the epidermis in the presence or absence of added vitamin A; but the vitamin reduced the incorporation of tyrosine in the superficial cells, and greatly diminished the uptake of cystine throughout the epithelium; these effects are probably correlated with the inhibition of keratinization. The uptake of inorganic sulphate was studied since in animals it is incorporated into mucopolysaccharides but not into amino-acids. In the deeper layers of the epithelium there was little difference in uptake between the A-treated and control explants, but in the superficial cells incorporation was very slight in the keratinizing controls but rapidly increased in the A-treated skin as secretory activity developed. This suggests that in the normal skin the basal cells have a mechanism for synthesizing mucopolysaccharides, that this is blocked by keratinization but that it continues to act when keratinization is stopped by excess vitamin A. It was interesting that whereas in the controls the uptake of tritium-labelled thymidine was restricted almost entirely to the basal nuclei, in the A-treated epidermis labelled nuclei occurred at all levels. It is unlikely that any of these histochemical changes represent the fundamental action of vitamin A on the epidermis.

Another group of chemical compounds that readily produce metaplastic changes *in vivo* are the carcinogens.

Spontaneous Transformation in Cell Cultures

Finally, a brief reference will be made to a rather different type of transformation that is well known in cell culture work. To prepare cell cultures, tissues are dissociated by enzymatic digestion, and the liberated cells are grown in flasks, tubes or bottles in an undifferentiated, very actively multiplying state, sometimes for many years. In order to survive indefinitely under these very unnatural conditions, the cells adapt themselves in various ways, so that usually they come to differ widely in appearance, behaviour and metabolism from cells of the same histological type freshly isolated from the body.

An interesting and important feature of these so-called transformations in long-term cell cultures is that they sometimes end in malignancy. Dr. George Gey[6] maintains two strains of rat fibroblasts derived from the same explant: one produces malignant tumours when implanted into rats, the other does not. Dr. Sanford and her colleagues, working in Dr. W. Earle's laboratory, have two strains of cells, both

descended from the same single mouse fibroblast'. After 1½–2 years in culture, one of these sister lines, called the 'high' strain, when grafted into mice produced lethal sarcomas in 97 per cent of the animals, while the other, termed the 'low' strain, produced sarcomas in only 1 per cent of the mice. The two strains differ in habit of growth and in metabolism, that of the 'high' strain being largely anaerobic and that of the 'low' strain almost normal, yet their antigenic properties are the same and either can immunize against the other.

Conclusions

How far are we justified in using the term 'cellular transformation'? Tissues certainly are transformed, but are the individual cells?

I know of no example of a structurally differentiated cell being directly changed into one of a different histological type. In the early embryo, a wide spectrum of developmental changes can be experimentally induced in the tissues, because all the component cells are at a very early stage of differentiation. When older tissues are subjected to morphogenic influences, the fully differentiated cells are not transformed but usually degenerate and are shed. The metaplastic change in the tissue is due to the fact that the structurally undifferentiated germinative cells are potentially capable of following more than one developmental path; which path they choose depends on their threshold of response to the particular environmental conditions to which they are exposed. In the normal animal, a striking instance of the germinative cells of an epithelium switching alternately from one developmental pathway to another is provided by the vagina: during dioestrus the basal cells differentiate into mucous elements, but when exposed to the influence of oestrogen they form a squamous, keratinizing epithelium instead, and the mucous cells are shed.

As Dr. Paul Weiss[8] has pointed out, the germinative cells of older tissues are not really undifferentiated, since their developmental repertory, though wider than is sometimes realized, is nevertheless extremely limited as compared with that of early embryonic tissues.

Personally, I do not think that we can consider this switching of germinative cells from one developmental pathway to another as a transformation in the strict sense of the word. As regards the type of 'transformation' that occurs in unorganized cell cultures, it is still uncertain whether the changes that appear in the cultures represent a real transformation of the cell population as a whole, or whether they are due to the selection of variant cells that are peculiarly well adapted for growth in this grossly abnormal environment. I think that sometimes, at least, selection is the more probable explanation of the phenomena observed.

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FOURAH BAY COLLEGE: UNIVERSITY COLLEGE OF SIERRA LEONE

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ON January 28, His Excellency Sir Maurice H. Dorman, governor of Sierra Leone and deputy visitor of the College, presented the Royal Charter to Fourah Bay College, incorporating it as the University College of Sierra Leone. Thus was inaugurated a new phase in the development of the College, although it has functioned as a university college for more than eighty years.

Fourah Bay College itself was founded in Freetown in 1827 by the Church Missionary Society. Before that, in 1816, a precursor of the College, the 'Church Institute', had been founded by the Church Missionary Society in the village of Leicester, just outside Freetown. This became a 'Seminary' in 1819 and moved to another village, Regent, in 1820. Its main function, and that of the early Fourah Bay College, was the training of evangelists in the belief that any continuous evangelistic work in West Africa should be undertaken by Africans.

The ambitiousness of the establishment of the College may be gauged from the fact that although a township with European traders had been established on the site of Freetown in the fifteenth century, the Colony of Sierra Leone was only established in 1808, with a population mainly of freed slaves who were brought from Nova Scotia in 1792 (they had fought for the British in the American War of Independence and were dissatisfied with their rewards of grants of land in Nova Scotia) and from Jamaica in 1802. In the following years the population was increased by a large number of Africans liberated from captured slave ships. Most of these were not acceptable by the more cultured repatriates from the United States and were established in villages along the coast of the Colony and in the hills above Freetown.

In 1827 the College was established with six students in a house that had at one time housed a slave dealer. Though numbers were small, the students soon achieved prominence in West African affairs. One of the first students was Samuel Crowther, who qualified, became a teacher for some years, and then returned to the College as a tutor. In 1841 he

and the Rev. J. F. Schon led the first Niger Expedition, and on his return he went to England, where he was ordained in 1843. He returned to Sierra Leone, and then proceeded to his native Nigeria, where he pioneered the spread of Christianity, and was consecrated Bishop of Lagos in 1864—the first African bishop of modern times.

During the Victorian era, the College was cosmopolitan, drawing its tutors from England, Africa, the United States and Germany; the first Principal was a Swiss. But teaching was not the sole occupation of the staff. Grammars, dictionaries and translations of the African languages came out of Fourah Bay. Of these, Koelle's "Polyglotta Africana" (1854), a comparative study of a great number of West African languages, is still a basic work.

By the early 1840's the number of students was more than thirty and the accommodation too cramped. A new building was initiated and was completed in 1848. This was sited on the isthmus between Fourah Bay and Destruction Bay (where the captured slave ships were broken up). This building, which still stands, housed the College for nearly a hundred years.

Fig. 1. The Students' Union. On the left is one of the original buildings of the hospital; on the right part of the new Union building. In the foreground is the Assembly Arena (Photo: T. Lloyd)

In 1870, the Rev. R. Sunter became principal, and he inspired the Church Missionary Society to extend the scope of the College to include the liberal arts as well as classics and theology. Suggestions that Fourah Bay College should be affiliated to an English university were made, and in 1876 affiliation to the University of Durham was established, whereby students could be admitted to any degree, diploma or licence of that University. At this time Sunter introduced extra-mural classes and some science teaching with the aid of Colonial surgeons who became part-time lecturers. Mathematics, and a little later geography, were subjects for degree courses.

In those days optimism in Sierra Leone was abundant, and the country was talked of as the place where West African development would start. There was even talk of a West African university developing from the College. The graduates of Fourah Bay College, with the standing of a British university degree, went out into the West African world and prospered, filling important posts in government, law, teaching, medicine, and the church.

However, the missionary finances started to dwindle, the Government did not recognize a great responsibility towards education, and the municipality of Freetown did not then feel a civic urge to develop or even maintain the College. Consequently the College was hard put to maintain itself; but it persevered with an average of twenty students until the end of the Second World War.

The first 'science' lecturer was appointed in 1924 and the foundation stone of a small block for science teaching was laid in 1925. From that time the establishment of the College has included a 'science' lecturer. This development was inspired and made possible by the bequests of two Africans: Dr. Obadiah Johnson and Dr. John Randall. It would seem that from 1929 the science lecturer was occupied with a few lectures given to the arts students, and with the non-graduate teacher training course which started in that year. In 1939 a course leading to the Durham Higher School Certificate was started with the hope that this would develop into a Faculty of Science. In 1941 the first students passed in botany, chemistry, physics and zoology—the teaching in all these four subjects being done by one lecturer.

On the outbreak of the Second World War the College buildings were requisitioned by the military authorities, and teaching continued in huts. In 1942 the College moved to Mabang in the Sierra Leone Protectorate some forty miles from Freetown. Here conditions were very primitive, science work proved impossible, and the science lecturer transferred to Government service and started the first formal sixth-form course in science at the Government Secondary School, Freetown. This lecturer was Dr. E. Downing, who eventually left Sierra Leone in 1946, but who returned in 1954 as head of the Department of Chemistry and dean of the Faculty of Science.

In 1945 a Commission to investigate higher education in West Africa, under the chairmanship of Sir Walter Elliott, visited the British West African Colonies, and as a result of this report, University Colleges and Colleges of Arts, Science and Technology were set up in Nigeria and the Gold Coast. When the Commission visited Mabang, economic conditions there were so difficult and the number of staff and students so reduced that they were not impressed and felt that the College was an uneconomic proposition and should be disbanded. This view was vigorously fought by two members of the Commission, Dr. E. H. Taylor-Cummings of Freetown and Sir James Duff, warden of the Durham Colleges. As a result of lengthy negotiations, a new ordinance was published in 1950 in which a largely autonomous College was set up, governed by a Council representative of Government, the Missions, the College teaching staff and other local interests. Financial responsibility was taken over by the Sierra Leone Government, which had the advice of the Council for Overseas Colleges of Arts, Science and Technology. The courses in the College were restricted to those already

Fig. 2. The new building housing the Department of Zoology and part of the Department of Botany (Photo: T. Lloyd)

existing, namely theology, arts and economics as degree courses, a postgraduate diploma in education, a nongraduate teacher-training course, and science courses to General Certificate of Education (advanced level).

An Education Commission under the chairmanship of Mr. John Fulton (then vice-chancellor of the University of Wales) visited Sierra Leone in 1954 to inquire into the general educational needs of the country and to make recommendations for a long-term policy for the development of Fourah Bay College. In spite of restrictions, the College had grown in numbers. As a result of this the Commission suggested an expansion in the fields of pure and applied science and the goal of university status as an ultimate objective.

A further Commission under Dr. C. H. Wilson, vice-chancellor of the University of Leicester, reported in 1959, and in accordance with the recommendations of this Commission a request was submitted that the College be granted a Royal Charter incorporating it as the University College of Sierra Leone, and the Inter-University Council took over from the Council for Overseas Colleges of Arts, Science and Technology. At the same time the College's responsibility for nongraduate teacher training was transferred to a new and separate Teacher Training College. Now the College consists of Faculties of Arts, Economics, Theology, Pure Science and Applied Science, as well as a postgraduate Education Department and an Extra-Mural Department.

In 1946 the College had returned to Freetown from Mabang and exchanged its old site (where the Queen Elizabeth II Quay was built) for an old military hospital on Mount Aureol, a considerable area of plateau and hillside. The accommodation on this site was either in old stone buildings or temporary wooden structures. With the aid of grants from the Colonial Development and Welfare Fund, the Sierra Leone Government, and local firms, especially the Sierra Leone Development Co., new buildings designed by Mr. Frank Rutter are slowly replacing the old. One of the first priorities in the rebuilding has been new buildings for the science departments, and most of these are now completed (Fig. 2).

In 1955 there was one lecturer in each of the subjects of biology, chemistry and physics, and a teacher of general science, who ran a preliminary course with which to feed the science course. The Faculty of Science was then established containing the Departments of Botany, Chemistry, Geography, Mathematics, Physics and Zoology. Now each of these has a staff of three with the exceptions of Geography (two) and Mathematics (five). At the same time a Department of Applied Science was established, where students take a diploma in engineering, which was established after consultations with the Departments of Engineering, King's College, Newcastle. More recently the preliminary course in general science was discontinued, as the number of students who have taken sixth form science has increased.

Science teaching is concentrated now on the general B.Sc. degree of the University of Durham. The immediate developments envisaged are the consolidation of the present courses and departments, and the addition of honours degrees.

At the moment there are some 350 students registered in the College. As the College is fully residential, the number of students is at present regulated by hostel accommodation, though this is being increased in the near future. Students from Sierra Leone are given preference in acceptance, provided they are suitably qualified. At the moment about half the student body is Sierra Leonian, with a few students from Ghana and Gambia, and the rest from Nigeria. This large Nigerian population is in part a reflexion of the traditional association of that country with Fourah Bay College when the College was the only institution providing a university education in West Africa.

In the science departments a number of research projects are under way, most of them dealing with local conditions.

The biological departments have a wealth of material literally at their doorsteps—a forest reserve only 50 yd. from the Botany Department is being established. Research in the Botany Department under Dr. F. J. Taylor is being directed towards the physiology of the local flora and of freshwater algae, experimental taxonomy of the local flora, the ecology of soil fungi, and the ecology and microbiology of mangrove swamps. The head of the Zoology Department, Mr. J. Phipps, has been studying the local grasshoppers intensively, and other research in that Department includes the study of mud wasps with their spider food, and the nitrogen metabolism of stick insects. The Botany and Zoology Departments have recently established a Marine Biology Laboratory on the coast some eight miles from the College.

The Chemistry Department, under Dr. E. Downing, is interested in the chemistry of natural products, immediately in waxes and their component acid and alcohols. Future lines of development in this Department are likely to be influenced by the parent University.

The two main lines of research being established in the Physics Department (head of the Department, Mr. E. G. Dunstan) are the study of the Earth's magnetic field, which has developed out of studies carried out in Nigeria during the International Geophysical Year, and the study of atmospheric electricity, for which the tropics are especially suited.

In the Geography Department, under Mr. G. Dalton, the main topics of study at present are climatology and land-use surveys. A somewhat related topic under study in the Department of Applied Science, with Mr. B. Pescod, is the nature of lateritic soils, especially with regard to the application of cement stabilization techniques.

The conferment of university college status leads to the hope that Fourah Bay College will attract research workers in science wishing to work in the tropics. From the point of view of the biological field worker, for example, Freetown offers a unique annual rainfall regime on the coast of West Africa, and a range of varied habitats within relatively easy reach.

OBITUARIES

Academician I. V. Kurchatov

THE death of I. V. Kurchatov on February 7 is a severe loss to physics, particularly in the U.S.S.R. As director of the Atomic Energy Institute of the Academy of Sciences and an outstanding leader in atomic energy research of all varieties, he played a leading part in determining Russian atomic energy policy. Much credit must go to him for the rapid post-war developments of the Russian programme, and he received many honours from the Soviet Government for his work. He was a member of the Praesidium of the Academy of Sciences and a deputy to the Supreme Soviet of the U.S.S.R.

Born in 1903 in Eastern Russia, Igor Vasilevitch Kurchatov graduated at the University of the Crimea in 1923 and started research at the Leningrad Physico-Technical Institute, then under the direction of A. Joffe, in 1925. Up to 1933 he carried out experimental and theoretical studies of dielectrics, particularly on the properties of Rochelle salt. He was the first to give a mathematical theory of ferro-electricity, basing his approach on the Langevin–Weiss theory of ferromagnetism. His many researches on this subject were summarized in a short book published in 1933. Other work at this time included studies of dielectric breakdown.

Kurchatov's nuclear physics work began in 1933, and in 1938 he was made director of nuclear physics research at the Leningrad Institute, where he and his collaborators conducted many pioneer researches into nuclear reactions produced by neutrons. His work on the activities induced in bromine, together with the results obtained by Fermi's group, led to the first identification of a long-lived nuclear isomer. Other work included detailed studies of the $^{10}B(n,\alpha)$ reaction, and the scattering and absorption of neutrons in water, paraffin and other moderating media. His group was thus exceptionally well placed to follow up the discovery of nuclear fission in 1939, and in 1941 he published an authoritative paper surveying various possible ways of developing a chain-reacting system based on thermal neutron fission of heavy elements.

The Atomic Energy Institute was started towards the end of the Second World War. It is a large establishment, occupying several hundred acres on the outskirts of Moscow, devoted to fundamental research on atomic energy. The wide scope of research there was revealed at the first Geneva Conference on the Peaceful Uses of Atomic Energy in 1955. From his public statement in 1958 claiming Russian priority in the development of a practical military form of the hydrogen bomb, it appears that Kurchatov played a leading part in military as well as civil applications of atomic energy.

In recent years, the problems of plasma physics and controlled thermonuclear reactions formed a significant part of the work at Kurchatov's institute. Studies of magnetic confinement of plasma were vigorously pursued there by a group led by a pre-war Leningrad colleague, L. A. Artsimovitch. The first public account of this work was given by Kurchatov at Harwell in May 1956, in a lecture remarkable not only for its content but also for the bizarre circumstance that his audience was at that time keeping work in this field secret. In 1958 he gave the first account of further work in his institute on this subject, including the building of the enormous magnetic trap installation *Ogra*.

Kurchatov's career is largely synonymous with the development of atomic energy in the U.S.S.R., and although he died before many important aspects have come to fruition, the Russian achievements in this field, together with the size and vitality of his research institute, stand as an impressive testimony to his abilities. He believed in the value of international collaboration in science, and gave a most friendly reception to visitors from England to his institute.

His high scientific abilities, integrity and personal charm greatly impressed all who met him.

R. S. PEASE
B. F. J. SCHONLAND

Prof. H. G. Robinson, C.B.E.

HENRY GOLAND ROBINSON, first professor of agriculture in the University of Nottingham, for many years principal of the Midland Agricultural College and later director of the University of Nottingham School of Agriculture, died on February 20 at his home in Wellington, Shropshire, aged sixty-three. A graduate of the University of Durham, he held appointments at Cockle Park and the then University College of Reading, before becoming senior lecturer in agriculture at the Midland Agricultural College, Sutton Bonington, in 1925. Ten years later he was appointed principal of the Midland Agricultural College, and led the developments which culminated in its union with the then University College of Nottingham as the Faculty of Agriculture and Horticulture. Robinson became the first professor of agriculture and dean of the Faculty.

Robinson will long be remembered for his work for the Midland Agricultural College and the University of Nottingham School of Agriculture, and for his

services to agricultural education and farming in Britain, for at one time he was a member of thirty-nine committees, including the Nottinghamshire War Agricultural Executive Committee and several of its sub-committees. He lectured on aspects of agriculture throughout Britain and was a keen advocate of good husbandry. For his services to agricultural education he was appointed a Commander of the Order of the British Empire in 1955, and he was elected emeritus professor of agriculture in the University of Nottingham on his retirement, through illness, in 1954.

J. D. Ivins

NEWS and VIEWS

First Award of the Vetlesen Prize : Prof. Maurice Ewing

Dr. Maurice Ewing, director of the Lamont Geological Observatory, Columbia University, New York, has been awarded the Vetlesen Prize for outstanding achievement in the earth sciences. This is the first award of this Prize, which consists of a gold medal, 25,000 dollars and support of publication of the recipient's scientific papers. Dr. Ewing, professor of geology at Columbia, and a native of Lockney, Texas, is known internationally for his work in the Earth sciences, and among the previous honours he has received are the Day Medal of the Geological Society of America ; the Agassiz Medal of the U.S. National Academy of Sciences ; and the William Bowie Medal of the American Geophysical Union. Dr. Ewing, who has been a teacher of both physics and geology, considers himself primarily a physicist who applies fundamental science—physics, chemistry and mathematics—to the study of the Earth.

The Vetlesen Prize was established this year at Columbia University by the G. Unger Vetlesen Foundation for "achievement resulting in a clearer understanding of the earth, its history or its relation to the universe". Like the Nobel Prizes established more than fifty years ago, the Vetlesen Prize recognizes no national boundaries, and any person in any country may be nominated for it. The Nobel Prizes, set up when the Earth sciences were of secondary importance, cover the fields of physics, chemistry, medicine, literature and peace. Funds for both prizes have been provided by Scandinavians. Alfred B. Nobel was a Swedish munitions maker. Georg Unger Vetlesen, a shipping executive, was a native of Norway who became a United States citizen during the Second World War. He established the foundation bearing his name shortly before his death in 1955. The Vetlesen Prize is to be awarded every two years provided a worthy candidate is presented.

The British Museum (Natural History) : Sir Gavin de Beer, F.R.S.

The retirement of Sir Gavin de Beer from the directorship of the British Museum (Natural History) at the end of April this year ends one of the most memorable decades in the history of this institution. He took office at a time when the Museum was still suffering from the effects of the War and during his tenure has succeeded in carrying out an ambitious programme of reconstruction and extension of the Museum facilities and also helped to restore its international prestige. The building of the North Block, with Lecture Theatre, Map Room, General Library and Reading Room, is one of the more obvious additions ; but the Mammal Building, extension of the Whale Hall, completion of the Entomological Block, and the new Botanical Gallery, with Cryptogamic Herbarium and laboratories, have all greatly increased the amenities and facilities for scientific study. The Mammal Balconies now include exhibits on the functional morphology of mammals, and the Central Hall has been re-organized to accommodate the big pachyderms and a completely new set of exhibits on evolution which were specially prepared in connexion with the Darwin-Wallace Centenary.

Sir Gavin has carried out investigations on *Archæopteryx*, and the evolution of Ratites, apart from many historical studies of special interest to the Museum, including the Darwin manuscripts and note-books ; Sir Hans Sloane and the British Museum ; the Banks correspondence ; and he initiated the Historical Series in the Museum Bulletin. Among his other publications a "Short Guide to the Museum", "Scientific Research in the Museum", and a "Handbook to Evolution" were issued for the use of visitors. It was a fortunate coincidence that the Darwin–Wallace Centenary should have occurred during the term of office of one of the greatest authorities on evolution and he took a leading part in the celebrations of that event. In addition, Sir Gavin was president of the fifteenth International Congress of Zoology, held in London during 1958, which attracted by far the largest attendance on record. He was also president of Section D (Zoology) at the meeting of the British Association in Oxford in 1954.

Sir Gavin de Beer's successor will be Dr. T. C. S. Morrison-Scott, director of the Science Museum. Dr. Morrison-Scott was formerly on the staff of the British Museum (Natural History), where he worked mainly in the Mammal Department (see *Nature*, 177, 1061 ; 1956).

Laboratory of the Government Chemist : Mr. E. H. Nurse, C.B.E.

On March 31, Mr. E. H. Nurse will retire as acting Government Chemist from what was until recently the Department of the Government Chemist. Mr. Nurse has spent the whole of his career in this Department, which he joined in 1915, following graduation with first-class honours in chemistry from the University of London. During the First World War he served for two years with the Royal Naval Air Service and the Royal Air Force as a hydrogen officer with airships. On the re-organization of the Scientific Civil Service in 1946 he became a principal scientific officer, and he was promoted to the grade of senior principal scientific officer in 1948. He has represented the Department on a number of scientific and technical committees and has been particularly concerned, both at headquarters and the subsidiary laboratories maintained at certain ports, with chemical work in connexion with revenue duties of Customs and Excise. He was appointed Deputy Government Chemist in 1954 on the retirement of Dr. J. R. Nicholls, and on the death of Dr. G. M. Bennett, in February 1959, he became acting Government Chemist. During his period as head of the

Laboratory he has seen its transfer from the Treasury to the Department of Scientific and Industrial Research. He was created C.B.E. in 1958.

Dr. D. T. Lewis

Dr. D. T. Lewis, who has been appointed Government Chemist, was born in Breconshire in 1909 and graduated at the University College of Aberystwyth with first-class honours in chemistry in 1930. He afterwards gained the degrees of Ph.D., and D.Sc., of the University of Wales. Prior to the War, he occupied various teaching posts and held lectureships at the University Colleges of Aberystwyth and Cardiff. In 1941, Dr. Lewis joined the Armaments Research Establishment of the Ministry of Supply and was associated with research and development work on conventional armaments. Leaving this work he was appointed one of the early members of Sir William Penney's atomic weapons team, and for the past seven years he has held the post of senior superintendent of the Chemistry Division at the Atomic Weapons Research Establishment, Aldermaston. In addition to his duties at Aldermaston he has also taken part in overseas trials in Australia and at Christmas Island. He has published a large number of papers in the various scientific journals dealing with inorganic physical and analytical chemistry. He has also published "Ultimate Particles of Matter", a book designed as an introduction for laymen to nuclear and associated sciences. Dr. Lewis is chairman of the Thames Valley Section of the Royal Institute of Chemistry and has been a representative of the Atomic Energy Authority on the board of governors of the Newbury Technical College.

Lucas Heights Research Establishment, Australia: Dr. G. C. J. Dalton

Dr. George Clifford James Dalton has been appointed director of the Lucas Heights Research Establishment of the Australian Atomic Energy Commission. Dr. Dalton was born at Te Awamutu, New Zealand, in 1916 and was a Rhodes Scholar in 1936. From Oxford he went to the Royal Air Force where he was occupied with radar research. At the end of the Second World War he went to Harwell, where he was in charge of the Fast Reactor Group of the United Kingdom Atomic Energy Authority. This Group carried out the early scientific work which led to the decision to construct the fast breeder reactor at Dounreay. During 1949–55, he was professor of mechanical engineering at Auckland University, New Zealand. Dr. Dalton joined the staff of the Australian Atomic Energy Commission in 1955 as chief engineer and deputy chief scientist.

Second Nuclear Reactor for Lucas Heights

A second nuclear reactor is being installed at Lucas Heights by the Australian Atomic Energy Commission. In announcing this, the Minister for National Development, Senator Spooner, explained that it will be a small and simple apparatus by comparison with the Commission's first reactor, *Hifar* (see *Nature*, 181, 1433; 1958). It will be used in the Commission's general programme for the development of a high-temperature gas-cooled reactor and will be complementary to *Hifar*, which was a 10,000-kW. materials testing reactor used also for making radioisotopes. Production of isotopes, which has already begun, forms an important part of the Lucas Heights programme. The new reactor will produce 10 kW. and will be employed for many tests and measurements where the intense radiation of *Hifar* is unnecessary. These will include physics studies of reactor material, and sample cores (fuel assemblies) for future power-reactor systems. Because of its simplicity and inherent safety of operation, the new reactor will also be used for training staff who will eventually work on other reactors. It is expected that the cost of installing the new reactor and its associated facilities will be in the region of £65,000.

The Game Research Association

A national organization to be known as the Game Research Association has been formed, by a responsible group of farmers, landowners and others interested in game conservation, to promote game research in Britain. The Association will be financed entirely by donations and membership subscriptions, and will carry out research into all factors controlling the game population of the country. The subjects to be studied, as funds and staff become available, include ecology of partridges and pheasants in relation to agriculture, forestry and other land use, regarding game as a natural resource; and also the more immediate problems of game mortality such as gapeworm, the effects of toxic chemicals and effective re-stocking methods. Laboratories for a temporary research headquarters are being loaned by Imperial Chemical Industries, Ltd., at Fordingbridge. The president of the Association is Mr. Harold Macmillan, and vice-presidents, Sir John Ruggles-Brise and Major John Morrison; chairman of council, Lord Porchester. Mr. A. D. Middleton, director of the Imperial Chemical Industries Game Research Station, Fordingbridge, is honorary research adviser, and Mr. F. O. G. Lloyd is honorary secretary–treasurer (temporary London office at 7–8 Great Winchester Street, London, E.C.2).

The I.C.I. Game Research Station, Fordingbridge

The work of this Station at Fordingbridge, in Hampshire, will continue, but with some reduction in the research projects and more emphasis on advisory and educational work. Research will include methods of artificial propagation and population dynamics. The advisory staff will continue, through personal visits, literature and other means, to give practical application to the knowledge which has been gained during fourteen years of work at Fordingbridge and, in pre-war years, in Hertfordshire and other places. Naturally, Imperial Chemical Industries, Ltd., welcomes the formation of an independent Game Research Association, which should be able to expand research in this field. The Fordingbridge team will collaborate in every possible way in the work of the Association.

Research on Grouse

In addition to the Game Research Association, and the work of the Imperial Chemical Industries Game Research Station, a third research project, concerning grouse, is now firmly established. The ecological study of grouse in Scotland, under the direction of Prof. V. C. Wynne-Edwards, of the University of Aberdeen, financed for the past three years by the Scottish Landowners Federation, is now being taken over and expanded by the Nature Conservancy. This is to be part of a wider project known as the Unit of Grouse and Moorland Ecology, the first of such units to be operated by the Conservancy. Its research results, from a long-term study of grouse population dynamics, will inevitably be of

permanent value to grouse management, which is an important feature of moorland economics.

State Aid for Museums and Art Galleries of Britain

For many years the Museums Association, through a succession of presidents and other officials, has emphasized the desirability—indeed the absolute necessity—of giving some measure of financial assistance to museums and art galleries, especially to the smaller provincial institutions. On February 26, Sir Edward Boyle, Financial Secretary to the Treasury, made a statement in the House of Commons which indicates that H.M. Government is at last fully alive to the present needs of museums and art galleries. There was a practical result in that various grants were announced. First was the direct provision in the Estimates for the national collections, which is to show an increase of £350,000 or 13 per cent. This welcome news will allow the British Museum to appoint fifty extra staff and enable the authorities to keep the Reading Room open to a later hour on, say, two evenings a week. Until 1959 the Victoria and Albert Museum, by means of its Circulation Department, was enabled through a Treasury Grant to disperse the hopelessly inadequate amount of £2,000 per annum to local museums for the purchase of specimens. Last year this sum was increased to £15,000, and now it is announced that the amount has been raised to £25,000. From the professional point of view, it was especially welcome news that the Minister of Education has decided to ask Parliament to approve of an entirely new type of grant to the Victoria and Albert Museum for the benefit of a provincial gallery. By this means it will be possible for Liverpool to purchase the "Holy Family" by Rubens.

It has been continually urged by the Government that the museum problem should be settled locally, and to this end the South Western Museum Regional Council was formed in January 1959. Its aim was to promote closer co-operation between museums, to improve the technical facilities available and to distribute financial assistance to museums and art galleries within the region. It was hoped that the Financial Secretary would be able to make a definite statement regarding assistance to this regional scheme, especially in view of the strong support given only the day before in a memorandum by the Association of Municipal Corporations. Unfortunately he was not able to announce any grant in this connexion. But perhaps the most welcome result of the debate in the House was the statement that the Government now realizes that many museums and art galleries in Britain are inadequately provided for, and that a general inquiry would serve a useful purpose. To this end the Chancellor of the Exchequer has invited the Standing Commission on Museums and Art Galleries to consult the Museums Association and others to consider the desirability of a complete review of provincial museums and art galleries. It is to be hoped that this review will take place in the foreseeable future.

Employment of Scientists in the United States

A report issued by the National Science Foundation gives final information on about 116,000 employed scientists (out of about 127,000) in the National Register of Scientific and Technical Personnel for 1954–55, roughly half of all American scientists at the time (American Science Manpower: Employment and Other Characteristics, 1954–55. Pp. vi+48. (N.S.F. 59–39.) Washington, D.C.: National Science Foundation, 1959). The largest group (41,000) was employed in chemistry and chemical engineering. About half of the 116,000 were employed in private industry and nearly one third by educational institutions. About 50,000 (44 per cent) were engaged in research, development or field exploration, about 20,000 in management or administration and about the same number in teaching. Nearly 40 per cent of the scientists held a doctorate and more than 33 per cent a master's degree. In 1954–55 the median annual salary for scientists reporting this item was 6,525 dollars and, in general, salaries were highest for scientists with a doctorate and those employed in private industry. About 8,000 (about 7 per cent) of the scientists were women, who were employed chiefly in the biological sciences, chemistry and psychology. Of the 127,000 respondents in the 1954–55 Register, more than 90 per cent were civilian scientists employed in scientific or in non-scientific specialities, including education, social work, and humanities. Of the remainder, about 4,000 were on active military duty, 4,200 students, 700 unemployed and 2,000 retired. These groups are not covered in the report.

U.K. Government Relief for Scientific Societies

The annual report for 1959 of the Parliamentary and Scientific Committee, besides a concise summary of the addresses and discussions during the year, records that the Committee's Rating Sub-Committee welcomed the recommendations of the Pritchard Committee insofar as they offer a 50 per cent rate relief to scientific societies and similar bodies, and extends to industrial research associations the same degree of rating relief as applies to industry in general (pp. 28. London: Parliamentary and Scientific Committee, 1960). Subject to certain reservations, the Committee hopes that the necessary legislation will be introduced by the Government at the earliest possible opportunity. First, the Committee regrets that the Pritchard Committee's recommendations, if implemented, will impose a material rate burden on those scientific organizations which have obtained total exemption under the Scientific Societies Act, 1843, and will also debar from such full relief other scientific societies which might have been able to qualify for exemption under that Act at some future date. The Committee recommended accordingly that if the Government did not find it possible to enable scientific societies to continue to enjoy full rating relief, arrangements should be made by the Minister for Science to afford assistance to scientific societies which will be rendered less effective by the implementation of the Pritchard Committee recommendations. Secondly, the Committee submits that certain modifications in the precise recommendations of the Pritchard Committee will be necessary to ensure that some scientific societies are not debarred from the rating relief recommended by reason of the definition of what is to constitute a charity for the purpose of rating benefit.

Vegetable Research

The Research Station at Wellesbourne, with its sub-station at Paglesham, Essex, was established in 1949 and has now a considerable volume of results (Ninth Annual Report, 1958, of the National Vegetable Research Station, Wellesbourne, Warwick. Pp. 55. 1959). A long-term assessment of chemical, physical, biological and ecological changes involved

in raising soil fertility to the high level required for vegetable production shows that farmyard manure exerts the greatest single effect. For some crops, however, the greatest yield is only obtained by supplementing with fertilizer. More detailed chemical investigations showed that there was an accumulation of sucrose, fructose and glucose, and a decrease in phosphorylated intermediaries, in the roots of beet immediately before flowering.

The report describes many studies on competition between weeds and crop, and the effects of pre-planting treatments. Various agents for weed control are under investigation, but it is interesting to note that the mere fact of growing vegetables for three years has reduced the number of weed seeds in the soil to about one-sixth the original number. Studies on the control of environmental conditions include extensive work on irrigation, and lettuce particularly benefited from adequate watering through its period of growth. Disease studies are now extensive, but perhaps the most significant findings are that silvering disease of beet can be controlled by seed treatment with streptomycin, the effectiveness of aldrin in reducing club-root disease, and the use of zinc frit for the control of powdery mildew of turnips and cabbage. Entomological investigations are concerned mainly with cabbage root fly, carrot fly and the root aphid of lettuce, while in methods of control, seed treatment and soil incorporation figure largely. Plant breeding is perhaps slow to give immediate results, but the report shows useful progress with many vegetables; in this, as indeed in other sections, reference must be made to the report itself, and it is clear that as the years go by it will become more and more valuable.

Plasma Physics and Thermonuclear Research

THE new section, Part *C*, of the *Journal of Nuclear Energy* is to be published quarterly and is devoted to plasma physics, accelerators and thermonuclear research (Pergamon Press, 4–5 Fitzroy Square, London, W.1). As Sir George Thomson explains in his brief foreword to the first issue (1, Nos. 1/2, October 1959), plasma physics is part of that study of gaseous discharges to which physics owes the fundamental discoveries of electrons and of isotopes, and from which it is hoped to be able to solve the problem of obtaining controlled energy from fusion reactions between nuclei of isotopes of hydrogen. Prof. M. S. Livingston in his foreword explains that accelerator technology has contributed significantly to the newer technology of thermonuclear science, and therefore the new journal will perform an important and useful function in sponsoring the merger of the two technologies with the study of plasma physics. In addition to eight original contributions, the October issue contains abstracts in English, prepared by the U.S. Atomic Energy Commission, of articles from "The Physics of Plasmas", published by the U.S.S.R. Academy of Sciences, a collection divided into four volumes in which are described the theoretical and experimental investigations carried out during 1951–58 in the Institute of Atomic Energy of the U.S.S.R. Academy on controlled thermonuclear reaction and associated subjects. Other features of the issue are translations of articles from *Atomnaya Energiya* and a list of titles of current papers and reports on plasma physics, accelerators and thermonuclear research appearing in some 50–100 journals published throughout the world. The October list covers publications since January 1, 1959. The editor-in-chief of Part *C* is Dr. J. V. Dunworth.

Russian Chemical Journals

THE Chemical Society announces that cover-to-cover translations of two additional Russian chemical journals are to be published with the assistance of the Department of Scientific and Industrial Research. The *Russian Journal of Physical Chemistry* (*Zhurnal Fizicheskoi Khimii*) is being published by the Society in translation starting with the issue for July 1959. It is intended that subsequent monthly issues will appear regularly, and it is hoped that the interval between the receipt of the Russian original and the publication of the translation will eventually be reduced to about three months. Mr. R. P. Bell is scientific editor of the translation. Another journal, *Uspekhi Khimii*, will be published monthly in translation under the title *Russian Chemical Reviews*, starting with the issue for January 1960, which it is hoped to make available in April. The scientific editor of the translation will be Dr. J. N. Agar, assisted by Dr. A. R. Katritzky and Dr. R. H. Prince. Translations for these journals are supplied for the Society by Infosearch, Ltd., and distribution is undertaken by the Cleaver-Hume Press, Ltd. Subscription inquiries should be addressed to the sole distributors, Cleaver-Hume Press, Ltd., 31 Wright's Lane, London, W.8.

The United States National Museum

IN a comprehensive report for 1959 it is stated that the site near the Washington Monument is now being prepared for the proposed Museum of History and Technology (The United States National Museum. Annual Report for the year ended June 30, 1959. Pp. vi+178. Washington, D.C.: Government Printing Office, 1959). The policy of this Museum is described as "to illustrate by means of the historic collections in the Smithsonian the cultural and technological development of the Nation since Colonial times". The plans include some thirty-eight major halls which have been coherently related to show a logical sequence of events. The needs of the individual museum visitor have been kept in mind, for it is conservatively estimated that some five million persons will enter the building each year. Provision is made for adequate air conditioning for the protection of objects as well as the comfort of visitors, circuits for television and electronic guide devices, and other electrical and plumbing devices in this great modern display unit. The plans thus indicate a museum building that will for the first time allow the great collections of the Smithsonian to be viewed in an adequate manner. During the sixth year of the continuing modernization programme work has also moved steadily forward on the other two fronts, namely, the renovation of the permanent exhibition halls in existing buildings and assistance to other branches of the Smithsonian Institution in the planning and presentation of exhibits.

Proteins from Grass

PIRIE and other scientific workers have directed attention to reserves of protein available in grass and other chlorophyll-containing material normally consumed as animal foodstuffs, but potentially of use to man. The efficient production of good-quality edible protein from such sources depends on the solution of various biochemical engineering problems which have been investigated by the Rothamsted

group for some years. A recent report from British Glues and Chemicals, Ltd., reflects the increasing interest in leaf protein; the Chayen impulse process, introduced a few years ago by this firm for the disintegration and extraction of bones and animal fats, has now been applied to a variety of other materials, including oilseeds, such as groundnuts, and grasses. The principle of this method lies in the use of shock waves of sufficient intensity and frequency to burst the tissues and cells of biological materials; it is illustrated by the depth-charge technique used in anti-submarine warfare and by the method of fishing with the aid of a dynamite charge. The report states that 100 tons of fresh grass (of 80 per cent water content) treated by the Chayen method yields about 2¼ tons of edible protein together with two important by-products—7 tons of fibre (suitable for the production of hardboard) and 0·6 tons of a 'chlorophyll syrup' containing fat-soluble vitamins, pigments and steroids. The commercial development of this process will be watched with interest by all who are concerned in any way with the nutritional problems of tropical and other areas, and it is to be hoped that the method can be introduced into those regions where additional supplies of supplementary protein are most needed.

Department of Scientific and Industrial Research: Studentships and Fellowships

The Department of Scientific and Industrial Research, which this year has awarded studentships to 2,143 research workers, as well as 271 advanced course studentships and 48 research fellowships, at a cost expected to exceed £1 million, and grants totalling £2,238,000 to 287 investigators at universities, technical colleges and similar institutions for researches in the natural and human sciences and technology, has now issued two publications replacing the former "Notes on D.S.I.R. Grants to Graduate Students and Research Workers". "D.S.I.R. Studentships and Fellowships" describes in detail the different types of studentships and fellowships in science and technology offered by the Department, including those tenable abroad and also the science studentships and fellowships administered on behalf of the North Atlantic Council (pp. 24. 1*s*. 6*d*. net. D.S.I.R. Research Grants. Pp. iv+10. 1*s*. 3*d*. net. London: H.M. Stationery Office, 1960). "D.S.I.R. Research Grants" gives similar information about the grants for special researches awarded by the Department and includes a note on the scheme of Senior Visiting Fellowships instituted by the Organization for European Economic Co-operation which the Department operates.

Gassiot Research Fellowships in the Meteorological Office

The official list of the functions of the Meteorological Office includes "Research in Meteorology and Geophysics". In the long history of the Office, 'geophysics' has come to mean terrestrial magnetism and seismology, and continuous observations in these fields have been made for many years at Kew, Eskdalemuir and Lerwick. In the past two decades the demands of meteorology have been such that it has not been possible to do much more than to maintain and publish the observations, especially in seismology. It has long been recognized that this is not a desirable state of affairs, and an important step towards the revival of research in the Meteorological Office in both fields has now been taken by the creation by the Secretary of State for Air of two research fellowships (named after John P. Gassiot, F.R.S., who in 1871 bequeathed to the Royal Society a large sum of money for the maintenance of magnetical and meteorological observations at Kew) in geomagnetism and seismology, respectively. The fellowships, which are tenable for seven years with a possible extension to ten years, will allow the holders to pursue any studies falling within the acknowledged fields of the two disciplines, with the aid of facilities provided by the Meteorological Office. It is also intended that there will be close contact with universities. Selection of the Fellows will be made in association with the Royal Society.

Gift to the Rensselaer Polytechnic Institute

A gift of one million dollars has been pledged to the Rensselaer Polytechnic Institute by Mr. and Mrs. Erik Jonsson, of Dallas, Texas, through the Jonsson Foundation, to help finance a new Science Centre at Rensselaer. Mr. Jonsson is chairman of the board of Texas Instruments, Inc. The gift, one of the largest single grants recently received by the Institute, is for construction of one unit of the Science Centre on the Rensselaer campus.

University News: Birmingham

Under the policy of general expansion throughout the University of Birmingham, it is now announced that the Faculty of Commerce and Social Science will be accommodated in a completely new building, and plans are in preparation with the view of commencing building work in 1961 and completing it in July 1962. Work on the £1 million building for the Department of Biology will start in mid-1960 and will be fully completed by 1963.

Dr. J. T. Davies, lecturer in chemical engineering in the University of Cambridge, has been appointed to the chair of chemical engineering and to the headship of the Department of Chemical Engineering from October 1, 1960. The following appointments have also been made: Dr. Gillian Vaisey, to be lecturer in the Department of Civil Engineering; G. Lees, to be lecturer in road materials in the Department of Civil Engineering; D. R. Milner, to be Lucas Fellow in metal joining in the Department of Industrial Metallurgy. A readership in reactor physics has been conferred on Dr. J. Walker, senior lecturer in physics, and in social medicine on Dr. C. R. Lowe, senior lecturer in social medicine.

Leeds

Appointments to professorships are announced as follows: Dr. J. Nutting, as professor of metallurgy from a date to be arranged; Mr. D. R. Wood, as professor of pharmacology from September 1; and Mr. J. M. Cameron, as professor of philosophy. Major grants to the University are: by the Department of Scientific and Industrial Research, £40,000 to the Department of Physics for research on cosmic ray showers, £5,650 to the Department of Leather Industries, and £2,200 to the Department of Electrical Engineering; by the Ministry of Aviation, £2,000 to the Houldsworth School of Applied Science for research on the fatigue properties of ferrous and non-ferrous alloys; by Imperial Chemical Industries, Ltd., £1,500 to the Department of Inorganic and Structural Chemistry to support X-ray structure analysis; and by the Hickson's Timber Impregnation Co. (G.B.), Ltd., £1,000 to provide a fellowship in the Department of Botany.

South Africa and Commonwealth Scholarships

Mr. I. F. A. de Villiers, First Secretary in the Office of the High Commissioner in London for the Union of South Africa, writes: "The article in *Nature*, of January 30, p. 271, on 'The Wandering Scholar in the British Commonwealth', mentions references, in debates in both Houses of Parliament, to the non-participation of the Union of South Africa in the Commonwealth Education scheme. I am concerned that this may have conveyed the incorrect impression that South Africa does not intend to participate; the actual position is that while the South African Government was not able to give consideration to the proposals of the Oxford Commonwealth Education Conference until quite recently, it has in fact decided to participate in both the Commonwealth Scholarship Plan and the Commonwealth Education Liaison Committee."

Announcements

Prof. Leo Szilard, professor of biophysics at the University of Chicago, has been awarded the Albert Einstein Gold Medal and Award for 1960. The Award itself is valued at 5,000 dollars, and is presented annually with the Medal.

The award of the Birbal Sahni Medal for 1959 has been made to Prof. P. Parija. The award was instituted by the Indian Botanical Society through a grant of Rs. 2,500 made by Prof. T. S. Sadasivan (Madras) in 1957 in memory of the late Prof. Birbal Sahni. The Medal is awarded annually in recognition of services to botany in India.

Mr. R. M. Wynne-Edwards, joint managing director of Constructors, John Brown, Ltd., has been appointed chairman of the Building Research and Road Research Boards for the period April 1, 1960–March 31, 1965, in succession to the two present chairmen, Sir Herbert Manzoni and Mr. E. John Powell, who have completed their terms of office.

The editorial office of *The Biochemical Journal* has moved from the Lister Institute to 133–135 Oxford Street, London, W.1, where all further communications should be sent.

By the generous benefaction of Prof. R. L. Wain, professor of agricultural chemistry in the University of London (Wye College), an income from the patents on his discoveries in the field of selective herbicides has been made available to the Agricultural Research Council and has been used to establish the Wain Trust Fund. One of the objects of the Fund is to facilitate the interchange of scientists between universities in the United Kingdom and overseas. The Council can now make available annually one to two awards (depending on the sums involved) to members of university staffs in Britain who wish to spend a period abroad. Applications or inquiries should be made to the Secretary, Agricultural Research Council, Cunard Building, Regent Street, London, S.W.1.

The forty-fourth annual meeting of the Federation of American Societies for Experimental Biology will be held in Chicago during April 11–15. Further information can be obtained from Sidney S. Negus, Medical College of Virginia, Richmond, Virginia.

The spring meeting of the Photobiology Group will be held at the University of Reading during April 1–2. Further information can be obtained from Dr. D. Vince, Department of Horticulture, University of Reading, at Shinfield Grange, Shinfield, Berks.

The Department of Chemical Technology of the Bradford Institute of Technology is organizing a symposium on Fluorescence and Fluorescent Compounds on May 6. Further details can be obtained from the Registrar, Institute of Technology, Bradford, 7.

It is announced that the third international congress in Photobiology is to be held in Copenhagen during July 31–August 5. The last date for registration is April 1, and further information can be obtained from Dr. B. C. Christiansen, Finsen Memorial Hospital, 49 Strand Boulevard, Denmark.

The eighth conference of the British Agricultural History Society will be held during April 7–9 at Harper Adams Agricultural College, Newport (Salop). Further information can be obtained from the Secretary of the British Agricultural History Society, Department of Agriculture, University of Oxford.

The Institution of Mining and Metallurgy will hold an international Mineral Processing Congress at Church House, Westminster, London, S.W.1, during April 6–9. Further information can be obtained from the secretary, B. W. Kerrigan, Institution of Mining and Metallurgy, 44 Portland Place, London, W.1.

The Faraday Society has announced that a general discussion on Oxidation Reduction Reactions in Ionizing Solvents will be held in the University of Durham, King's College, Newcastle upon Tyne, 1, during April 11–13. Further information can be obtained from the Assistant Secretary, Faraday Society, 6 Gray's Inn Square, London, W.C.1.

The second International Spring School of Physics of the Istituto di Fisica Theorica of the University of Naples will be held during April 20–May 7. The school is sponsored by the Società Italiana di Fisica and the University of Naples, and is to receive a grant-in-aid from Nato. Applications must be sent to the director of the School not later than March 31.

The sixty-fifth annual congress of the South-Eastern Union of Scientific Societies will be held during April 22–25. Lectures and excursions will be held covering the biology, zoology, geology and archæology of the south-eastern counties; visits to various museums in the region will also be made. Further information can be obtained from F. Edwards, 53 The Drive, Shoreham-by-Sea, Sussex.

The annual conference of the Ergonomics Research Society will be held in Cambridge during March 28–31. The topics to be discussed include ergonomics in the Armed Forces, in building research and athletics; and ergonomics in the Netherlands. There will be a symposium on factors in prolonged work, especially inspection. Further particulars can be obtained from Mr. D. U. Hunt, British Iron and Steel Research Association, Park Lane, London, W.1.

The Annual Easter Congress of the Universities Federation for Animal Welfare will be held at Saltley College, Birmingham, during April 8–12. The programme includes a symposium on Humane Experimental Technique and lectures on introducing animal welfare to Libya (Dr. F. Jean Vinter), aspects of meat production (D. Norma Egginton) and humane slaughter (Colonel D. J. Anthony). Further information can be obtained from UFAW (Easter Congress), 7*a* Lamb's Conduit Passage, London, W.C.1.

DEVELOPMENT OF WOOD-USING INDUSTRIES

UNDOUBTEDLY among the most significant happenings of the past twelve months for the future of forestry and timber in Great Britain has been the publication of two reports on economic studies carried out by a Canadian firm of consulting engineers, Messrs. Sandwell and Co., Ltd., of Vancouver. These reports are entitled "Small Pulp Mill Survey" and "Board Mill Survey", respectively, the former having been conducted under the auspices of the Organization for European Economic Co-operation, the United Kingdom being one of seven member countries studied, while the latter was undertaken for selected regions in Great Britain at the request of the Forestry Commission*.

There are two reasons why such surveys were called for. First, the wood-pulp industry in Europe is very largely concentrated in Scandinavia, the remaining countries importing either pulp or materials made from it, such as paper or fibreboard; naturally, it was desirable to see if something could be done in the home country to reduce dependence on imports and to develop new industries. Secondly, as a consequence of the extensive afforestation programmes of the past three or four decades, a very large volume of wood is becoming available, mostly from the small trees removed in the thinnings that must be carried out to make it possible for the trees retained in the forest to grow to saw-timber size within a reasonable time. This amount is not only already large, but also is increasing annually—and will continue to do so for a long time yet—while one of its main markets, namely, pit-wood for the coal mines, is approaching saturation; Scotland's needs are already met entirely from Scotland's own forests, and the demand is showing signs of falling off.

Basic to these studies are the facts that Britain imports three-quarters of a million tons of paper and boards out of her annual consumption of 4 million tons (1956 figures), and production in Britain of the balance is dependent on the import of 2 million tons of pulp. Expressed otherwise, three-quarters of the wood that is consumed by the British paper industry is imported.

It has always been recognized that for a pulp mill to be profitable there are several essential requirements which are not easy to fulfil. Only three of these requirements need be mentioned here: (1) a large and regular supply of suitable wood; (2) the cost of that supply delivered at the mill must be low compared with the price that is paid in the existing markets for such material for other uses such as pit-wood, light poles and box-wood; (3) a good water supply with effective means of disposal of effluents.

The consultants have tried to answer two main questions: (1) Given a delivered cost for wood, what is the minimum capacity of a pulp mill to be economically feasible under any of the processes available? (2) If the output is to be as low as 30 tons per diem, at what price must wood be available? It is not possible here to discuss the details; but their findings are that a separate plant set up solely to produce ground-wood (that is, mechanical) pulp is out of the question; that for a chemical (bleached sulphate) pulp plant receiving its raw material at a price that would be viewed as so low as to be doubtfully attainable by United Kingdom growers—though it is the average top price prevailing in North America—namely, £8 10*s.* a ton, the plant would have to be able to turn out at least 80 tons of pulp a day. If its capacity were as low as 30 tons a day, the price that it could afford to pay for the wood would be altogether impossibly low.

The overall conclusion is that if Britain is to develop in this field, her pulp mill must be integrated with other wood-based industries, notably with paper-making, like the recently opened hardwood pulp mill at Chepstow. Integration with saw-milling and connected industries such as veneering, plywood and furniture would also be helpful by providing an appreciable proportion of the raw material from waste available on the spot at a very low cost. If this can be done, a relatively small mill of 30–40 tons capacity should be able to pay a price for the rest of its wood which, though still lower than is currently being obtained, can be viewed as not impossibly so.

It is estimated that by 1965 two centres in Scotland (Inverness and Fort William) would probably be producing enough wood surplus within 100 miles radius by road to support a small-scale pulp mill if it can pay something like the current price for its wood, but probably only ten years later if its price is appreciably lower. At least two other centres are expected to have a similar surplus by 1975. It is known that a proposition to site such a mill in Scotland is under serious consideration by a leading group of wood industrialists. Incidentally, it has to be noted that our paper is mostly made of blended materials, including large amounts of straw—of which much more would be available if needed—and imported pulp of a type that would be selected in relation to the properties of that obtained from the local materials.

The second survey deals with the possible establishment of further hardboard, chipboard and insulating board mills, using the same raw material from the thinnings of our plantations. Although the amount of hardboard we import to-day corresponds to a production of 500 tons per diem, it is concluded that its manufacture would not be economically attractive unless the raw material could be cheapened to an extent that, as for the pulp mill, would only be attainable by integration with other wood industries, and this is not currently a practicable proposition with sawmilling because this industry is at present dispersed among a very large number of relatively small units. It is emphasized that chipboard and insulating board mills also require to be large to be reasonably profitable, with a daily output of at least 50 tons. They would be able to pay a rather higher

* (1) Forestry Commission. Small Pulp Mill Survey, United Kingdom—Economic Study. By Sandwell and Co., Ltd. Pp. iv+43. 4*s.* net. (2) Board Mill Survey, United Kingdom—Economic Study. By Sandwell and Co., Ltd. Pp. vi+70. (London: H.M. Stationery Office, 1959.) 5*s.* net.

price for their wood than that quoted for the pulp mill, a price that is still lower than the grower is at present getting, but within the range that he might be able to accept without putting himself out of business, provided every possible economy was made. Capital requirements would be about £1–2 million. In contrast with the prospects of further pulp mills, the most favourable area for board mills is considered to be southern England.

In the light of these surveys, it seems likely that Britain will have new wood-using mills of either or both types being built in the coming decade. There are not a few criticisms of the premises underlying these Sandwell reports with regard to costs, prices and trends, and suggestions that the size for profitability, at least for board mills, could be rather smaller and the capital cost less. However, it seems agreed that there must be a considerable reduction of the costs of growing and delivering the large amounts of wood required, and that there is certainly room for reduction by improved efficiency all along the line; there will be every incentive for cheaper production as other markets are bound to fall during what, without such mills, will be a period of large over-production. In all cases there will be marketing problems, especially in view of the free competition of imports under the Outer Seven trade agreements, but cautious optimism appears justifiable, and expansion in the directions indicated is to be expected in the near future.

H. CHAMPION

BIOCHEMISTRY AT THE IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY, LONDON

THE Imperial College of Science and Technology, London, has accepted a benefaction of £350,000 from the Isaac Wolfson Foundation to build and equip new laboratories for biochemistry and chemical microbiology and to support teaching and research in these subjects. Dr. E. B. Chain has been appointed to the chair of biochemistry and will take up the appointment in 1961.

This munificent benefaction will enable the College to erect a new building, to be known as the Wolfson Laboratory, adjacent to the Royal College of Science building in Imperial Institute Road. The Biochemistry Department will also occupy some laboratories in the Royal College of Science building shortly to be vacated by the Physics Department for its large new building in Prince Consort Road. Biochemistry at the College, which has been under the direction of a reader since the last occupant of the chair, Prof. A. C. Chibnall, succeeded Gowland Hopkins at Cambridge during the War, will thus burgeon out. The Department's new equipment will include fermentation units of comparatively large size and workshops for advanced mechanical and electronic equipment. It will provide accommodation for training and research in the neglected borderland between biochemistry and chemical engineering, and for research on an adequate scale on the biochemical production of chemicals of interest. Such a department, set in the Imperial College, with its very large school of engineering and flourishing schools of physics, organic chemistry and plant physiology, should find conditions highly propitious for major advances in biochemical knowledge.

Dr. Chain has since 1948 been at the Istituto Superiore di Sanità in Rome, where he has built up one of the best equipped, largest and most active centres of biochemical research in Europe. He has had there many of the facilities for which he had earlier, and unsuccessfully, pressed in Great Britain—in particular, equipment of pilot-plant scale for fundamental studies of substances of microbial origin and biochemical interest.

Dr. Chain, a graduate of the University of Berlin, was forced to leave Germany by Nazi persecution in 1933, and he became a British subject in 1939. He first worked under Gowland Hopkins at Cambridge, on snake venoms and phospholipids. In 1935 came an invitation from Prof. (now Sir Howard) Florey to join the scientific staff of the Sir William Dunn School of Pathology at Oxford, with the object of organizing a biochemistry section there. As University lecturer in chemical pathology he remained at Oxford until the end of 1948. His work there included a study of the biochemical mode of action of some snake venoms, on the mode of action of lysozyme, on the mode of action of the spreading factor, on tumour metabolism and on a rapid method for the determination of phosphate. In 1938, with Florey, a systematic study of anti-bacterial substances produced by micro-organisms was started. This led to the discovery of the curative properties of penicillin and heralded the era of antibiotics. In this work he played a leading part in the chemical studies on the isolation and structure of penicillin. For his part in the discovery of penicillin he was awarded the Nobel Prize for Medicine and Physiology in 1945, jointly with Sir Alexander Fleming and Florey. Dr. Chain was elected to fellowship of the Royal Society in 1949.

At the Istituto Superiore di Sanità, with the support of Prof. D. Marotta, director of the Institute, and the Italian Government, Dr. Chain has carried out research in many directions. His collaborators have included chemical, mechanical and electronics engineers, biochemists, organic chemists, microbiologists and geneticists. A wide range of subjects has been studied, mainly in two fields of biochemistry, chemical microbiology and intermediate carbohydrate metabolism in animals, touching on the methodological, biochemical and biological as well as the chemical engineering aspects of the subjects.

Among the biochemical subjects studied in the field of chemical microbiology have been factors involved in the biosynthesis of penicillin. The continuation of this work led to the discovery, by a team of research workers in the Beecham Laboratories in England, to which Dr. Chain has acted as adviser and consultant, that the main part of the penicillin molecule (6-aminopenicillanic acid) could be made by biosynthesis, and that this could be modified afterwards by chemical means. A great range of new antibiotics can be made in this way. They include a penicillin which is acid-stable and can be taken by

mouth and one which attacks staphylococci resistant to normal penicillin. Compounds of this kind open up exciting prospects in the antibiotics field.

Other studies conducted in Rome have been on the green iron-containing streptomycete pigment ferriverdin, on submerged kojic acid and citric acid fermentations and on the production of ergot alkaloid in submerged fermentation. Among the chemical engineering aspects of chemical microbiology there have been extensive studies on agitation and aeration. Biological studies have included investigations on the relations between morphology and metabolism in filamentous fungi and genetical problems in filamentous fungi. Studies on carbohydrate metabolism in animals have been concerned with the mode of action of insulin and the interrelations between carbohydrate and amino-acid metabolism in brain and nervous tissues.

DIRECTION OF SCIENTIFIC AND TECHNICAL RESEARCH IN FRANCE

A PUBLICATION, *French Science News* (2, April–June, 1959), published by the Direction Générale des Affaires Culturelles et Techniques for the Ministère des Affaires Étrangères, describes the organization which has been set up to determine policy for scientific and technical research throughout the country. Two high-ranking committees have been formed, the first being an Interministerial Committee, the members of which include the Prime Minister as chairman, the Minister of National Education, the Minister of the Armies, the Minister of Finance and Economic Affairs, the Minister of Industry and Commerce, the Minister of Agriculture, the Minister of Public Health, and qualified representatives of the French community.

The main tasks of the Interministerial Committee, which is responsible for proposing to the Government all measures for the development of scientific and technical research, are as follows:

"To maintain a fair balance between the amount of credits appropriated for the different fields of research;

"To develop to its maximum usefulness French national research, which presupposes a detailed study of the profession of a research specialist and the milieu in which research is performed;

"To anticipate new research possibilities which will benefit the nation, which presupposes long-term government options in the field of science."

The second is an Advisory Committee, the members of which are: Maurice Letort as chairman (Letort is scientific director of Research and Studies, Centre of Charbonnages de France); Prof. Pierre Aigrain, vice-president of the Paris Faculty of Science; Prof. Jean Bernard, Paris Faculty of Medicine; Prof. Rene Dumont, National Agronomic Institute; Prof. Paul Germain, Paris Faculty of Science; Rene Latarjet, co-director of the Radium Institute and the Curie Foundation; Prof. Andre Lichnerowicz, Collège de France; Maurice Ponte, general director of the Compagnie Générale de T.S.F.; Prof. Charles Sadron, Strasbourg Faculty of Science and director of the Centre of Macromolecular Research; Pierre Taranger, industrial director of the French Atomic Energy Commission; and Felix Trombe, research director at the National Scientific Research Centre (Mont-Louis).

The Committees are served by a common secretariat directed by a general delegate. The general delegate can form work committees for specific objects and composed of experts. He works in close co-operation with the general planning commissioner.

The journal is published quarterly by the Association pour la Diffusion de la Pensée Francaise, 23, rue La Perouse, Paris, 16e.

PRODUCTION AND CONSUMPTION OF ENERGY IN GREAT BRITAIN

DURING the past four years some remarkable changes have taken place in the consumption of energy in the United Kingdom. Indeed, since the War the situation in the whole of Western Europe has changed, from that of an energy-exporting economy to that of an energy-importing one. A few years ago there were fears of a shortage of energy in Great Britain. To-day there is the picture of rapidly rising coal stocks, and of real alarm in the mining villages.

Recently this subject was dealt with in an enlightening talk to the Fuel Luncheon Club by Sir Harold Hartley*, whose association with the international study of the energy problems of Western Europe entitle him to be listened to with earnest attention. His revelations should disturb any complacency with regard to the extent of our technological effort in the development of our coal resources.

The pattern of the energy consumption has changed quickly in the following respects in the past four years. Coal consumption fell 3 per cent per annum between 1955 and 1959, while that of oil rose by 12 per cent per annum. Electricity consumption continued its steady annual rise of 6 per cent, while gas declined by 1 per cent per annum. The competitive position depends upon factors of efficiency and of convenience, the relative basic prices of the therm in the primary forms of energy being: coal at the pithead, price 3½*d.*, at £10 per ton, 8½*d.*; fuel oil, at £10 per ton, 6*d.*; paraffin, at £20 per ton, 11*d.*; while gas at the average price costs 1*s.* 9*d.* per therm, and electricity at 1·55*d.* per unit, 3*s.* 9*d.*

* Talk to the Fuel Luncheon Club on January 19 on "Energy in the United Kingdon—the Changing Scene", by Sir Harold Hartley.

While stagnant demand has struck the coal-fields, technical advancement has raised the potential productivity of the deep mines to a figure of 3·86 tons per man-shift. This is a pointer to the possibilities of saving the competitive position of coal so far as regards price. The technological aspects offer greater possibilities, if adequately pursued. Thus, in the production of electricity the coal station can compete favourably with the nuclear energy station, because of the greater inherent efficiency that has been developed over recent decades through improvements in technique and design.

The same story of change and advancement could apply to the gas industry, since the technical outlook of the industry has changed radically. It is not likely that the gas industry will build in the future conventional carbonizing plants, for attention is now being turned towards the total gasification of coal, bringing into use new techniques applicable to the use of cheaper low-rank coals. With these there may well be combined processes involving the gasification of oil, and the use of imported liquid methane. With high-pressure gas generation, pipe-line distribution over long distances becomes practicable and economic.

In regard to oil, the question of availability has been changed by the outlook regarding the discovery of new sources of oil in the Middle East, Libya and the Sahara, and of large natural gas fields in the Pyrenees. Against this must be set the likely growth of demand for energy, as the under-developed countries in the world respond to modern standards of living.

Sir Harold Hartley, in considering the energy outlook, has attempted to sketch the future pattern of energy consumption in Britain. Some 280 million tons of coal equivalent will be required per annum by 1965. Of this, some 9½ million tons may come from nuclear energy, and 8 million tons in coal equivalents from hydro-electricity, coke and oil for generating power, leaving some 55 million tons per annum for steam generation by coal, an increase of some 10 million tons over 1959. The true forecast for the growth of other uses of coal, gas and oil offers a more difficult problem, and may well depend upon the pattern of technological advancement. Gas, provided it can be made at a competitive price, has potentialities in the domestic and industrial sphere, at three different levels of calorific value: a domestic gas at 500 or more B.T.U./cu. ft.; a synthesis or industrial gas of 320 B.T.U.; and a producer gas of 180 B.T.U./cu. ft., for which there are still uses, particularly in specialized fields and where the gas can be used, as in coke production, to free fuels of higher calorific value.

The competitive power of coal and its derived fuels can only be enhanced if the needed technological effort is put into the attempts to develop the new processes needed. Inevitably, the future demand will tend towards requiring energy either through a wire or a pipe, with any question of handling refuse or polluting the atmosphere excluded. Further, in the direction of the total gasification of coal lies the only hope of solving the problem of sulphur pollution.

In the matter of these potential fields of development an adequate tempo of research and development has been sadly lacking. Sir Harold voices the opinion that national policy in regard to research and development in the field of energy is badly out of balance. Very large sums of money and much available scientific effort are devoted to the nuclear field and insufficient of these resources to the utilization of coal, our greatest national asset.

R. J. Sarjant

HOST INFLUENCE ON PARASITE PHYSIOLOGY

THE sixteenth annual conference sponsored by the Bureau of Biological Research was held at Rutgers University, New Brunswick New Jersey, during January 29–30. The subject for discussion was host influence on parasite physiology.

The chair was occupied in turn by Dr. L. A. Stauber (Rutgers University), Dr. Norman Stoll (Rockefeller Institute) and Dr. Wm. Trager (Rockefeller Institute).

In his opening remarks, Dr. T. von Brand (Bethesda) observed that there was a time not very far back when a person interested in parasite physiology was regarded as an oddity. Now a 'physiological bandwagon' was emerging, possibly a reflexion of the brilliant advances being made in biochemistry. The study of parasite physiology, he considered, had changed in many ways; more people were interested and there was an emphasis on instrumentation, which demanded complicated apparatus, although man himself was the chief factor in any research. He recalled that during his youth in Germany, Weinland, that prince of experimenters, had been held up in his work on *Ascaris* metabolism for lack of a reducing valve. Distinct differences were apparent on the lines along which research on free-living invertebrates and parasites had developed. With the former the most significant advances were made by von Frisch in the field of sensory physiology. The study of parasites had developed along more chemical lines, possibly due to the fact that such early workers as Bunge and Weinland were interested primarily in chemical reactions. The biochemistry and physiology of parasites were initiated and extended in seeking to elucidate the mode of action of old or in the search for new drugs. Advances in our knowledge of host–parasite relationships followed. Non-biochemical studies of parasites were, however, of equal importance.

Dr. L. R. Cleveland (University of Georgia) then gave a paper on the effects of insect hormones on the protozoa of *Cryptocercus* and termites. This wood-feeding cockroach *Cryptocercus* has nine families, fourteen genera, and more than thirty species of flagellate parasites in its hind-gut. During each moulting period of a host all these species undergo sexual cycles. In the flagellates of adults and intermoult nymphal hosts, sexuality never occurs under natural conditions; when the insect growth and differentiation hormone, ecdysone, is injected into such hosts, gametogenesis is induced in their flagellates, and the time required for induction depends, within certain limits, on the amount of ecdysone injected. In an adult, 2,000 units will induce it in four genera within 3 hr.; 100 units will do the same in a 4th instar intermoult nymph.

Under natural conditions the sexual cycles of some genera of flagellates require six days, some nine, some twenty-six, and others 45–50 days for completion; 100 units of ecdysone, given to a 4th instar intermoult nymph, will bring all cycles to completion in seven days.

In intermoult nymphs and adults, injection of ecdysone produces sexuality in parasites without moulting of hosts.

Dr. J. D. Fulton (National Institute for Medical Research, London) spoke on some aspects of research on trypanosomes. The relationships of the three African trypanosomes, *T. brucei*, *T. gambiense* and *T. rhodesiense*, was first discussed. They cannot be distinguished morphologically and have sometimes been regarded not as separate species but as three biological races of a single species, *T. brucei*. Their distinguishing characters were dealt with in detail. The Tinde experiment started by Corson in 1934 had thrown considerable light on the affinities of these three parasites, on their physiological characters as well as on host–parasite relationships. The significance of polymorphism in trypanosomes and the presence of cytoplasmic inclusions, each character a facet of the host–parasite relationship, were discussed. The evidence suggested that sexual processes had not been demonstrated in these parasites. Dr. Fulton also described experiments on transformation in trypanosomes by means of deoxyribonucleic acid using drug resistance as a marker. The results obtained were negative or equivocal.

Dr. R. E. Hungate (University of California, Davis) described the factors influencing rumen protozoa. He showed how the ruminant provides to its symbiotic microbiota relatively constant temperature, moisture, osmotic pressure, *p*H, anaerobiosis, and food. The effect of variations in these factors on the protozoa was discussed, and the ability of the latter to withstand the normal variations in these factors was emphasized. In particular, the stress at the time of transfaunation was considered, including the devices for maintaining the necessary environment. The chief factor causing variation in the rumen microfauna is presumed to be differences in food. The effects of food may not be direct but mediated through bacteria which act upon it before they are consumed by the protozoa. The utilization of cellulose and the rapid ingestion of starch were stressed as characteristic of certain protozoa. The possible importance of protozoa during adaptation from hay to a high grain ration was presented.

Dr. A. R. Timms (Louisiana State University School of Medicine) dealt with the work of that School on schistosome enzymes. He explained how *Schistosoma mansoni* converts glucose quantitatively to lactic acid by the Embden–Meyerhof scheme of phosphorylating glycolysis which is also a major pathway for glucose utilization in mammalian tissues. However, enzymes from the parasite and the host, although catalysing the same biochemical transformations, are immunologically different.

Antimonials were shown by Bueding *et al.* to produce their antischistosomal activity, at least in part, by specific inhibition of phosphofructokinase activity of *S. mansoni*, leaving the host's phosphofructokinase largely uninhibited.

A protease was described which was thought to be in the gut of schistosomes, and which showed a marked specificity for hæmoglobin and globin when compared with other blood proteins. The possibility was discussed that this enzyme might provide an essential source of amino-acids for the parasite by degrading the host's hæmoglobin.

The paper by Dr. D. Fairbairn (McGill University, Canada) dealt with the physiology of hatching and larval exsheathment in nematodes. A result of investigations conducted in Canada and Australia has been that hatching and exsheathing of infective ascarid eggs and trichostrongyle larvæ can now be induced *in vitro* under conditions which closely resemble those in the host's intestinal tract. Under controlled conditions of *p*H, oxidation-reduction potential, temperature and concentration of free carbon dioxide, these processes occur at a rate comparable to that observed *in vivo*, and with identical morphological changes. Quantitative differences in the requirement of individual species for the components of this complex stimulus have been observed and positively correlated with conditions in the host. Exsheathment of *Haemonchus contortus*, for example, occurs only at high concentrations of free carbon dioxide such as are present in the sheep rumen, while a condition for optimal hatching of *Ascaris lumbricoides* eggs is that the carbon dioxide concentration be much lower, approximating that found in the small intestine of feeding mammals. The free-living infective eggs and larvæ cannot continue their development in the absence of the foregoing stimulus, which is in general peculiar to the host's intestinal tract, and thus ensures the transition to a parasitic existence. The processes of hatching and exsheathment constitute an internal response to stimulation, which is enzymic and results in digestion of the egg-shell and sheath.

The final paper, by Dr. P. P. Weinstein (Bethesda), was concerned with excretory mechanisms and excretory products of nematodes. The mechanism by which excretory products are released is poorly understood. Passage via cuticle, elimination by gut and so-called 'excretory system' may occur alone or in combination. This latter system was named primarily on teleological grounds, and little evidence for excretory function is available. Such a 'system' has been implicated in osmoregulatory activity and in moulting. Possible mechanisms for discharge of fluid such as secretion accompanied by preferential reabsorption were considered. The gut may play an important part in excretion of waste and the role of the cuticle and other structures was evaluated. The identification of the chemical nature of excretions and secretions was of possible importance regarding sensitization, development of functional immunity and pathological effects in the host. Products from axenically cultured parasitic nematodes are the only ones available for analyses. Much waste is apparently liberated as amino-acids and peptides or as organic acids, especially C_4 types. *In vitro* culture methods in defined media are urgently required for these studies.

A summary of the conference was given by Dr. Ernest Bueding (Louisiana State University) as follows. Since the occurrence of many biochemical reactions has been demonstrated in a large number of animal species of unicellular organisms and of plants, there has been a tendency to over-emphasize similarities and to overlook differences among various forms of life. Such biochemical differences may concern metabolic pathways and reactions (for example, fermentation products). In addition, it has been demonstrated that enzymes catalysing the same reactions in different species may not be identical with each other. Considerable biochemical differences have been uncovered not only between parasites and

their hosts, but also among various parasitic species, even though they may be related to each other morphologically and taxonomically. Therefore, in biochemical studies of parasites, similarities and differences must receive equal attention and any one-sided view will result in a distorted picture. It is suggested that comparative biochemistry should be concerned with the nature of biochemical variability from patterns common to many forms of life; this, in turn, should contribute to a better understanding of biochemical evolution to a parasitic form of life.

J. D. FULTON

VIBRATIONS: THEIR EFFECTS AND ANALYSIS

IN this technological age, in which larger and larger amounts of power are being harnessed to aid mankind, it is not surprising that the unwanted adjunct of power, vibration, is becoming of great importance. Thus, for example, it is not only the public itself which is annoyed and fatigued by the noise of jet aircraft, but also the fabric of aeroplanes is now tending to show signs of fatigue and to crack. Again, in the field of supersonic transport, the motion of the aircraft can be of a frequency (around 5 c./s.) at which the body is least attuned to absorb the vibrational energy imposed upon it.

These topics, together with the more industrial problems of machinery vibration and occupational diseases arising from excessive vibration of drills, etc., were the subjects discussed at the recent meeting of the Acoustics Group of the Physical Society, held on January 20, at the Imperial College of Science and Technology, London.

Dealing first of all with problems of the vibration isolation of machinery, Mr. P. H. Allaway (Absorbit, Ltd.), in a review paper, gave an excellent appraisal of the many types of isolating materials and systems now available. The effect of the rigidity of the ground or floor structure was discussed, together with the effect of damping in shock vibration isolation. He emphasized the need for choosing the right type of installation for any type of application, and showed in the ensuing discussion a wealth of valuable experience and 'know-how'.

Dr. John Agate (Ipswich and East Suffolk Hospital) presented a somewhat frightening picture of the influence of vibrations in industry on the hands of operating personnel. Four diseases were mentioned in all: cysts of carpal bones, osteo-arthritis, soft-tissue injuries and a circulatory disturbance known as Raynaud's phenomenon. The small cysts can only be seen on X-ray examination and are not of any significance. Osteo-arthritis of the elbows is, of course, not confined to people working with vibrating machinery, though there is ample evidence of this being a contributory cause. Raynaud's phenomenon, which Dr. Agate dealt with extensively, is a circulatory disorder of the blood stream in the hands, and it arises from their operating in an environment of heavy vibration. In such cases, there is a lessening of the blood stream in the small arteries of the hands, and it is typified by the fingers and even the whole hand becoming white or blue. It is difficult to schedule the disease as a disability, since most fingers show these symptoms in the cold; further, many workers using vibrational types of machinery do not suffer with this loss of circulation in the fingers in the warmth of their factories, but only show the symptoms later in colder conditions, and then about six to eighteen months after first exposure.

The prevention of this disease is not easy, since any frequency less than 600 c./s. causes the damage to the arteries, the range of 40–125 c./s. nevertheless being the most serious. The lesson to be learnt is, in fact, the need for automation for any processes of this kind. Since this can only be introduced in very special instances, the solution is still unavailable and needs further scientific study.

In view of the recent interest in supersonic transport aircraft, Flight Lieut. Guignard's description of the work of the R.A.F. Institute of Aviation Medicine on physiological effects of low-frequency vibration was both interesting and significant from the point of view of design. The jet liners of the present have a natural frequency of oscillation of the fuselage structure somewhere in the region of 4–6 c./s., and pilots placed in the cockpits of these aircraft have been known to suffer from the up-and-down movements of that part of the long fuselage. The experiments described illustrate the reasons for this, and emphasize the need for designing away from such frequencies. It is found (Fig. 1) that if a male person, in a relaxed sitting posture, is vibrated vertically through the seat, a resonance occurs at some 5 c./s., the amplification of the head and shoulders being as much as three times that of the seat movement. Above this resonance frequency, the damping in the body eliminates harmonics of higher frequency. The effect of tensing the body is favourable, increasing the resonant frequency to 6·3 c./s. and also increasing the damping, thus reducing the amplitude of head movement by a small though significant amount. At these frequencies around 5 c./s., tests in the United States indicate a serious reduction in performance with poor eye-correlation, fatigue and pains in the chest.

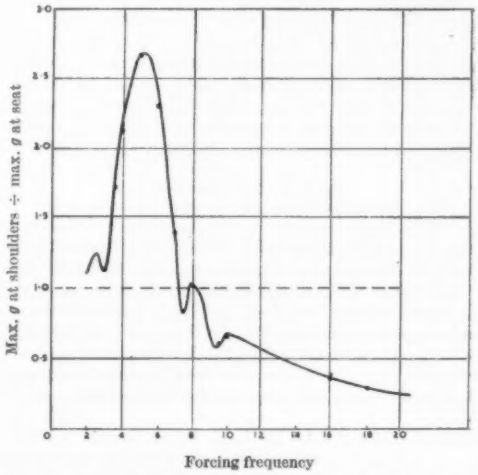

Fig. 1. Ratio of shoulder to seat acceleration plotted against frequency. Note the sharp resonance of the body at 5 c./s.

It is clear that this is a phenomenon of vital significance in the design of aircraft. The problem is not confined to aircraft, however. Ships cannot in any way claim freedom from vibrations of this frequency, while even trains, 'juddering' to a standstill in railway stations, set up exactly this type of disturbance.

Two complementary papers concerning the fatigue of aircraft structures due to vibrations set up by jet noise were presented respectively by Prof. E. J. Richards and Dr. B. L. Clarkson, of the Department of Aeronautics, University of Southampton. Jet noise arises from the turbulent motion of the jet gas as it mixes with the surrounding air. The total radiated energy is only a very small fraction of the energy of the jet, however (say, a hundredth of 1 per cent), and elaborate methods of experimentation have to be devised to measure the turbulence functions which are directly related to the radiated noise. In his paper, Prof. Richards described the space-time correlator and other apparatus used to obtain the spectrum of turbulence as seen by an observer moving with the jet stream. The relevant speeds of convection were discussed and a first attempt made to predict the radiated sound from the spectra of turbulence measured in this way.

There is, in general, no one discrete frequency of sound emitted from a jet. Consequently, the adjoining structure is vibrated randomly by the noise field and can in theory oscillate in an infinity of modes of oscillation. If a large number of modes do occur in practice, it is clear that the theoretical approach to prediction must be different from that adopted if the vibration is of a relatively simple kind. Dr. Clarkson's paper described experiments carried out on the vibrations of the rear part of the *Caravelle* airliner due to jet efflux, a programme carried out jointly by the firm, Sud-Aviation, and the University of Southampton. The analysis was concentrated on the strains in the centre of four panels of the fuselage skin aft of the engine nozzle; the first three being in line between two circumferential frames and the fourth being adjacent to the centre gauge of the first group but separated by a frame. Correlation measurements indicated that the lower frequencies (up to 500 c./s.) were associated with essentially overall vibration modes and have low strain amplitude. At the higher frequencies, having the larger strains, the frames tended to act as boundaries and the mode of vibration was confined to the stringers and panels between any two adjacent frames. In these measurements on this particular aircraft, the main resonance peak in each panel occurs at about 600–700 c./s. and has been identified with the fundamental stringer twisting mode (that is, adjacent panels are 180° out of phase). Strain response in the higher frequency range of 800–1,000 c./s. appears to be associated with a considerable number of closely spaced resonant frequencies.

This method of analysis using correlation techniques is a considerable step forward in the study of random vibrations of aircraft, ships and submarines, and the success outlined in the paper suggests that greater use should be made of this method of vibration analysis. E. J. Richards

A CONVECTIVE-TURBULENCE THEORY OF THUNDERSTORMS

By Dr. N. RAMALINGAM
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IT is well known among meteorologists that in practical forecasting of thunderstorms the methods in current usage, such as the parcel methods, etc., of analysis of the dry-bulb and wet-bulb soundings of the atmosphere plotted on $T - \varphi$ grams or other thermodynamic diagrams, are often unreliable.

The initiation of thunderstorms, at least in such cases that occur in a calm atmosphere over land on hot afternoons, as experienced over India in the hot pre-monsoon months, has been investigated from the point of view of modern knowledge about turbulence. In doing that, however, the limiting condition:

$$\frac{\rho_1 - \rho_0}{\rho_0} > \frac{27\,\pi^4 k \nu}{4\,g h^3} \qquad (1)$$

given by Lord Rayleigh[1] from his mathematical investigation of the motion in the Bénard cells formed, when a fluid of thickness h in equilibrium with its density ρ_1 at the top being greater than its density ρ_0 at the bottom breaks down into convection, is taken as the main physical basis. In the above expression ν is the kinematic coefficient of viscosity, and k is the coefficient of conduction of heat of the fluid.

Indeed, even so far back as 1925, Brunt[2] made it very clear that some of the phenomena associated with thunderstorms can be explained in the same way, and that the violence of thunderstorms would appear to indicate that a high degree of instability is built up before the breakdown occurs. This suggestion, however, does not appear to have been pursued quantitatively.

In his original paper, Rayleigh gave the limiting condition as:

$$\beta' r > \frac{27\,\pi^4 k \nu}{4\,h^4} \qquad (2)$$

where $\beta'(= -\beta)$ is the lapse-rate; and $r = g\alpha$, α is the coefficient of expansion of the fluid, and g is the acceleration due to gravity.

Since he was considering a fluid of small thickness h, he took:

$$\beta' = -\beta = \frac{\Theta_1 - \Theta_0}{h}$$

Θ being the departure from the equilibrium temperature, and:

$$r = g\alpha = g(\rho_1 - \rho_0)/\rho_0(\Theta_1 - \Theta_0)$$

hence, (2) reduces to (1).

If, however, we take a layer of air of thickness z, then we may take $\beta' = \dfrac{d\Theta}{dz}$; and from the relation $\rho_1 = \rho(1 + \alpha d\Theta)$ and taking $\rho_1 - \rho = d\rho$, we may

write : $r = g\alpha = \frac{g}{\rho}\frac{d\rho}{d\theta}$, so that (2) reduces to :

$$\frac{d\rho}{\rho} > \frac{27\,\pi^4 k\nu}{4\,g\,z^4}\,dz \qquad (3)$$

Since we are dealing with atmospheric air where the heat is gained only at the bottom near the ground, the rest of the motion being adiabatic, the last condition becomes :

$$\frac{dP}{P} > \frac{27\,\pi^4\gamma k\nu}{4\,g\,z^4}\,dz \qquad (4)$$

where P is the atmospheric pressure, and γ is the well-known adiabatic coefficient for air ($= 1{\cdot}4$). Since in the atmosphere, except very close to the ground, transmission of momentum and heat is brought about mainly by the turbulent eddies, the above limiting condition may be written as :

$$\frac{dP}{P} > \frac{27\,\pi^4\gamma K_M K_H}{4\,g\,z^4}\,.\,dz \qquad (5)$$

where K_M is the eddy viscosity and K_H is the eddy conductivity.

Since we are dealing with a large-scale phenomenon, such as the thunderstorm, much error may not arise, if, for simplicity, K_M is assumed to be nearly equal to K_H. Then from the expression for K_H quoted by Sutton[3], we may write :

$$K_H = l^2_H\sqrt{\left(-\frac{g}{\theta}\frac{d\theta}{dz}\right)}$$

where l_H is the mixing length and θ is the potential temperature. Further we take, with Prandtl, $l_H = \varkappa z$, where $\varkappa$ is the well-known von Kármán's constant ($= 0{\cdot}38$). Then the limiting condition (5) reduces to :

$$d\log P > \frac{27\,\pi^4\gamma\varkappa^4}{4}\,(-\,d\log\theta) \qquad (6)$$

Summing up for all possible eddies, Σ of left-hand side must exceed Σ of the right-hand side. In other words, integrating from some level, l, to the ground-level, 0, we get the critical condition for the convective turbulent breakdown in the atmosphere as :

$$\frac{\log\frac{P_1}{P_0}}{\log\frac{\theta_0}{\theta_1}} > \frac{27}{4}\,\pi^4\gamma\varkappa^4 \qquad (7)$$

(taking $\varkappa = 0{\cdot}38$, the right-hand side $= 19{\cdot}2$ which is rounded off as 19. If $\varkappa$ is taken as $= 0{\cdot}37$, the right-hand side could be taken as 17).

We therefore get the critical condition $\log\frac{P_1}{P_0}\Big/\log\frac{\theta_0}{\theta_1}$ should exceed 19 (taking $\varkappa = 0{\cdot}38$) for the breakdown in the equilibrium of the air to occur.

Since the left-hand side occurs as a ratio the logarithms may as well be taken to the base 10. Of course, to be more precise, one can take the potential temperatures corresponding to the two virtual temperatures. But this will not be of much significance. (Conversely, from a calculation of the left-hand side from the atmospheric sounding obtained before the occurrence of the thunderstorm, one can derive the value of von Kármán's constant by this independent method.)

For purposes of practical forecasting of thunderstorms while P_0 (about 1,000 millibars) refers to the ground-level, it will be sufficient if P_1 is taken as 500 or 600 millibars, since the lowest layer of 15,000 ft. or so only will be of importance ; θ_0 and θ_1 are the potential temperatures corresponding to the dry-bulb temperatures at those levels.

Examination of a few random cases of the actual soundings of the atmosphere taken before thunderstorms seem to confirm the validity of the above critical condition (7). The same critical condition also appears to be applicable to other thunderstorms other than of the simple type assumed.

If the early morning sounding shows the ratio to just fall short of 19, one may be able to forecast whether a thunderstorm is possible later in the day by merely predicting whether insolation will be able to raise θ_0, so that the ratio exceeds 19, as the only other variable θ_1(P_1 and P_0 already having been chosen by us) is likely to remain practically the same, unless there is reason for believing that the air mass would have altered much in the few hours.

Of course, for a correct application of the critical condition (7), the sounding must strictly be obtained from a direct vertical ascent, as the soundings normally obtained by balloons are really 'spread over' observations.

In passing, it may be mentioned that while in the parcel method, etc., the $T - \varphi$ gram is used as an energy diagram, in this case the $T - \varphi$ gram serves little purpose except perhaps as a nomogram to read off the potential temperatures, and to judge the moisture content.

It follows, incidentally, from the above investigation that, surprisingly, the moisture in the air apparently seems to play a minor, or subsidiary, part so far as the initiation of the thunderstorm is concerned. Examination of the $T - \varphi$ grams referred to above also seem to confirm this view. This, perhaps, seems to be the reason why in the parcel method, thunderstorms are found to occur even in cases when the latent instability, as shown by the positive area, is little or nil ; and vice versa. Lest it should be misunderstood, it is clarified further. Water vapour being a constituent of the air, it also partakes fully in the convective processes of the air as outlined above ; and once the breakdown occurs in the equilibrium of the air, the water vapour will also undergo convection with its attendant condensation and release of latent energy, which all go to aggravate further and accelerate the vertical motions. If the moisture content of the air particularly at the lower levels is large, as shown by the wet-bulb temperatures being closer to the dry-bulb temperatures in the soundings, then when the breakdown occurs, there will be greater condensation and greater release of energy resulting in violent vertical motions that result in the formations of great vertical columns of cumulo-nimbus clouds, showers and all other attendant phenomena normally associated with thunderstorms. If the moisture content is less, and still the critical number is exceeded, and the breakdown occurs, there will probably be only development of a few cumulus clouds ; while if the air is practically dry, then something like what is known among aviators as 'clear air turbulence' will presumably result.

More details of this investigation will be published elsewhere.

[1] Rayleigh, Lord, *Phil. Mag.*, **32**, 529 (1916).
[2] Brunt, D., *Nature*, **115**, 299 (1925) ; "Physical and Dynamical Meteorology", 2nd ed., 219 (1939).
[3] Sutton, O. G., *Quart. J. Roy. Met. Soc.*, **74**, 13 (1948).

VARIATION OF ELECTRON DENSITY IN THE IONOSPHERE WITH MAGNETIC DIP

By SHEILA CROOM, AUDREY ROBBINS and J. O. THOMAS
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THIS communication describes how the average ionospheric electron density (N_h) measured at local noon on quiet days in December 1957, at a series of fixed heights (h) in the F region, varies with the magnetic dip (I). The electron density profiles were deduced from observed $h'(f)$ curves by a method already described[1,2], the calculations having been carried out on the electronic digital computer, *Edsac II*, in the Mathematical Laboratory in the University of Cambridge.

It has been previously reported[3] that in September 1957 N_h varied with magnetic dip in an interesting and somewhat unexpected manner, and that the variation differed from that of the peak electron density N_mF2, particularly in the lower parts of the $F2$ layer. It was shown that, in these parts, the N_h (I) curve had maxima in N_h, where the dip was about 60° and there was evidence that the maxima occurred nearer the magnetic equator as greater heights were investigated.

Our previous investigations have now been extended to include the northern winter solstice, particularly in order to investigate whether N_h is abnormally large, corresponding to the well-known enhancement of N_mF2 described below.

When values of N_mF2 observed at different places are studied, two anomalies can be found: one, called the winter or seasonal anomaly, in which the values of N_mF2 are greater than expected on a simple theory in the winter hemisphere at medium and high latitudes, and the other, called the December or non-seasonal anomaly, in which, all over the Earth, the values measured in December are greater than expected. These variations have recently been studied in detail by Yonezawa[4]. At places in medium and high latitudes in the northern hemisphere, the two anomalies are in the same sense, so that the recorded values of N_mF2 are greater in December and January than at any other time of year.

Fig. 1 shows N_h at noon at a series of different heights plotted against magnetic dip for the month of December 1957, and may be compared with Fig. 1 in our previous communication[3], which was plotted for September 1957. The values plotted for N_h are the averages for all the good records for the ten International Quiet Days. The average values of N_h are estimated to be correct to within 5 per cent for stations in the northern hemisphere. The results for the southern hemisphere stations are probably somewhat less accurate. The observatories for which the points are plotted are listed in order of magnetic dip in Table 1.

The main features of the curves shown in Fig. 1 are the striking maxima in N_h, which occur at the larger values of h, in the form of a narrow peak centred on a dip of 70° (N.) and extending 10° on either side. The values of N_h at the 70° peak are probably exceptionally large as a result of the abnormally high sunspot number for this month ($\overline{R} = 239$).

Once it is realized that the winter anomaly in N_h may be restricted to a comparatively narrow

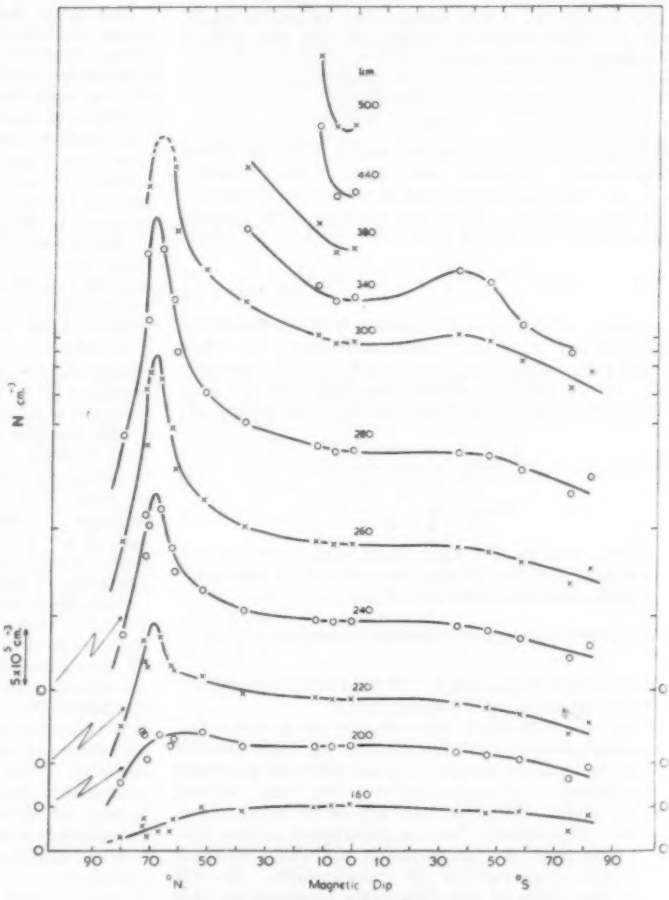

Fig. 1. Variation with magnetic dip of the mean quiet electron density N at a series of fixed heights in the F region at local noon in December 1957. The zero of the scale for the electron density at each height is marked. The stations used are listed in order of decreasing magnetic dip in Table 1

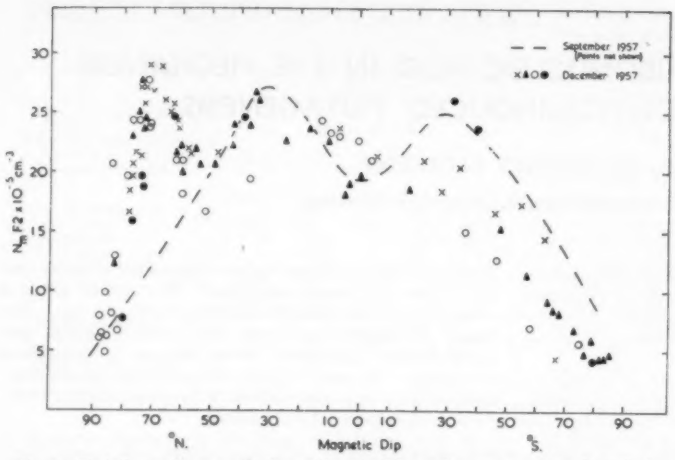

Fig. 2. Variation with magnetic dip of the monthly median noon values of N_mF2 in December 1957 for four geographical longitude zones: ×, 30° W.–50° E.; ▲, 50° E.–180° E.; ●, 180° W.–130° W.; ○, 13.5° W.–30° W. The broken line shows for comparison the variation of the monthly median N_mF2 for September 1957 (individual values are not shown)

range of dip angles, it is of interest to investigate how N_mF2, at the peak of the layer, depends on the dip in the same month. In Fig. 2 the monthly median values of N_mF2 for 12.00 L.M.T. are plotted against I, and it is at once evident that this quantity, also, exhibits the same comparatively narrow peak of increased ionization.

The monthly median values of N_mF2 have been separated in Fig. 2 into four main zones of geographical longitude. It is clear that the 70° peak in N_mF2 is independent of longitude. The broken line in Fig. 2 shows, for comparison, a smoothed curve of the variation of N_mF2 against dip in September 1957. This curve shows no indication of a peak

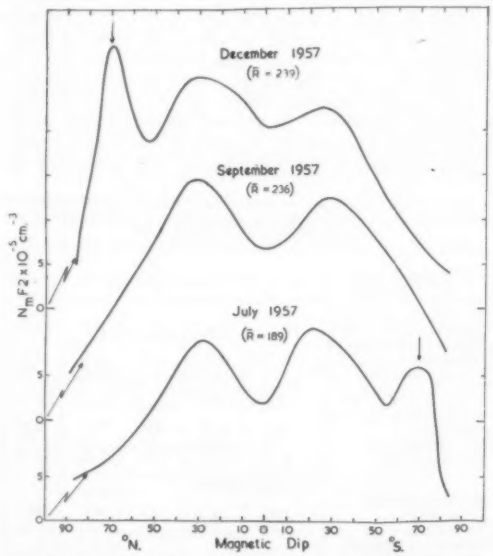

Fig. 3. Variation with magnetic dip of monthly median N_mF2 at local noon in July, September and December 1957. $\bar{R}$ is the monthly average relative Zurich sunspot number

near $I = 70°$ (N.). Results similar to those for December 1957 were obtained for the months of October and November 1957 and January 1958.

When values of N_mF2 are plotted against dip for other hours of the day and night, it is found that a similar maximum occurs near $I = 70°$ (N.) throughout the daylight hours. It appears at sunrise, is most prominent near noon and then decreases until at midnight it has disappeared.

Similar analyses carried out on observations for years with smaller sunspot numbers indicate that the size of the peak decreases with decreasing sunspot number.

A similar peak in N_mF2 occurs in the southern hemisphere in winter when the sunspot number is high. This is illustrated in Fig. 3, where a smooth curve has been drawn through the monthly median values of N_mF2 for July, September and December 1957.

A comparison of the variation of N_h with dip in December 1957 (Fig. 1) with the variation of N_mF2 for the same month (Fig. 2) indicates that, below about 300 km., there is no evidence in N_h of the minimum which occurs at 50° (N.) in N_mF2, and that N_h in this month decreases uniformly towards the magnetic equator from a dip of 60° (N.), as it did in September 1957 (Fig. 1 of ref. 3).

Table 1. Details of Stations for which $N(t)$ Data were Available
$N(h)$ profiles for stations marked C were computed at the Cavendish Laboratory. The results for stations marked S were taken from ref. 5

Station	Source	Geographical latitude	Geographical longitude	Magnetic dip
Point Barrow	C	71° 08′ N.	156° 48′ W.	80° N.
St. John's	C	47° 33′ N.	52° 40′ W.	72° N.
Washington	S	38° 44′ N.	77° 08′ W.	72° N.
Inverness	C	57° 27′ N.	4° 15′ W.	71° N.
Slough	C	51° 30′ N.	0° 36′ W.	67° N.
Adak	C	51° 54′ N.	176° 39′ W.	63° N.
San Francisco	C	37° 26′ N.	122° 10′ W.	62° N.
Puerto Rico	C	18° 30′ N.	67° 12′ W.	52° N.
Panama	S	09° 23′ N.	79° 53′ W.	39° N.
Talara	S	04° 34′ S.	81° 15′ W.	13° N.
Chimbote	C	09° 04′ S.	78° 35′ W.	07° N.
Huancayo	S	12° 03′ S.	75° 20′ W.	01° N.
Concepcion	C	36° 35′ S.	72° 59′ W.	36° S.
Port Stanley	C	51° 42′ S.	57° 52′ W.	47° S.
Port Lockroy	C	64° 50′ S.	63° 31′ W.	58° S.
Pole Station	C	90° 00′ S.		75° S.
Wilkes	C	66° 25′ S.	110° 27′ E.	82° S.

We are grateful to the Director of the Mathematical Laboratory of the University of Cambridge for permission to use *Edsac II* and to all the organizations, particularly the World Data Center *A*, Boulder, Colorado, U.S.A., which have lent us $h'(f)$ records. We should like to acknowledge the assistance of the computing staff of the Radio Group of the Cavendish Laboratory. This work was carried out with the aid of a grant from the Department of Scientific and Industrial Research.

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SIGNIFICANCE OF RIBONUCLEIC ACID IN THE MECHANISM OF FORMALDEHYDE-INDUCED MUTAGENESIS

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THE present article reports the significant occurrence that formaldehyde exhibits no mutagenic activity towards *Drosophila melanogaster*, by the larval feeding method, unless ribonucleic acid is present in the treatment medium.

In a study of the mode of action of chemical mutagens, the use of a chemically defined and axenic treatment medium is clearly essential for the precise definition and discrimination of both qualitative and quantitative effects. Such a medium has now been developed for *Drosophila melanogaster* by Sang[1], in which the dose-response for the main dietary constituents on the duration of larval life has been determined. On the basis of these findings, he has formulated an optimal medium (Table 1), which allows larval development to be completed in approximately 4·4 days; this compares with 4·1 days when the same strain is allowed to develop on an optimal supply of killed yeast. The omission of ribonucleic acid from the synthetic medium prolongs the period of larval development to about seven days[1]. Thus, although *Drosophila* larvæ can normally develop without an exogenous supply of ribonucleic acid, its addition accelerates development, indicating that preformed purines (or their nucleosides or nucleotides) are assimilated, to supplement or replace the natural synthetic process.

Table 1. Composition of Standard Culture Medium

	(gm.)		(gm.)
Yeast ribonucleic acid	0·4	Na_2HPO_4	0·189
Casein ('Genatosan-low vitamin')	5·00	Aneurin	0·0002
Fructose	0·75	Riboflavine	0·0010
Cholesterol	0·03	Nicotinic acid	0·0012
Lecithin	0·40	Calcium pantothenate	0·0016
Agar ('Oxoid-Kobe No. 1')	3·00	Pyridoxine	0·00025
$NaHCO_3$	0·14	Biotin	0·000016
KH_2PO_4	0·183	Folic acid	0·0010
		Water to 100 ml.	

The folic acid content of this medium is about ten times the minimum required in a medium containing ribonucleic acid, since it is known that the folic acid requirement is increased when ribonucleic acid is omitted from the diet. This excess does not interfere with development when optimal ribonucleic acid is supplied in the food.

The *Drosophila* stock used in the present study, and in previous experiments[3,4], the Oregon-*K* strain, does, however, require a dietary supply of cytidine for normal growth and development[2]; this was supplied as cytidylate (0·025 per cent). Since ribonucleic acid contains cytidylate, this was not added when ribonucleic acid was present. The medium will be referred to as the synthetic medium (*sm*) when ribonucleic acid is omitted, and as *sm* + ribonucleic acid when the acid is present. Ordinary medium is the yeast–maize meal–treacle medium normally used for culturing *Drosophila* in this laboratory. It was decided to omit the egg sterilization procedure and autoclaving of the medium normally essential with this technique, since formaldehyde itself effectively suppresses microbial growth, and propionic acid is used as a fungicidal agent, as in previous experiments. The procedure for treatment of larvæ and brood pattern determinations for sex-linked lethal mutation rates is as previously described[3]. The age of larvæ is counted from the time of hatching from the egg. The larval developmental time for treated larvæ was counted from emergence from the egg to puparium formation. In most experiments the larval developmental time is compounded of pre-treatment, treatment and post-treatment times.

It was decided to test the mutagenic activity of formaldehyde in the presence and in the absence of ribonucleic acid, now made possible by Sang's refined culturing technique.

Experiments were carried out at a constant concentration of formaldehyde ($2·0 \times 10^{-3}$ *M*) with different levels of ribonucleic acid in the treatment medium. The optimal concentration of the acid in the synthetic medium has been shown by Sang to lie between 0·4 and 0·7 per cent[1]. Table 2 shows the results obtained over the concentration range 0·2–0·6 per cent ribonucleic acid, where larvæ were kept on the treatment medium for the whole of larval life. The mutagenic activity of formaldehyde in the first brood is seen to be significantly lower at the lowest concentration of ribonucleic acid tested (0·2 per cent) than at the 0·3 per cent ribonucleic acid level ($\chi^2 = 15·36$ with one degree of freedom). The mutation frequencies of the first broods over the range 0·3–0·6 per cent ribonucleic acid are not significantly different from one another (heterogeneity $\chi^2 = 0·18$ with three degrees of freedom). Second broods are sampled as a check against possible changes in brood patterns by influences on the speed of germ-cell development; these are seen to be not significantly different from one another over the ribonucleic acid concentration range tested (heterogeneity $\chi^2 = 1·98$ with four degrees of freedom). It should be noted that in the formaldehyde-containing synthetic medium (at least, at the concentration used here), the larvæ do not

Table 2. Effect of the Concentration of Ribonucleic Acid on the Mutagenic Activity of Formaldehyde, when Treatment is for the Entire Larval Life

Formaldehyde concentration	$2·0 \times 10^{-3}$ *M*				
Ribonucleic acid concentration (per cent)	0·2	0·3	0·4	0·5	0·6
Larval developmental time (days)	6·5	6·0	5·5	6·5	7·5
Per cent survivors	75	80	58	54·5	65
	First broods				
No. chromosomes examined	602	598	632	336	326
No. lethals	18	54	54	26	38
Per cent lethals	2·99	9·03	8·54	7·74	11·65
	Second broods				
No. chromosomes examined	604	514	770	602	539
No. lethals	10	14	18	10	10
Per cent sex-linked recessive lethal mutations	1·65	2·72	2·34	1·66	1·85

Table 3. Effect of Ribonucleic Acid on the Mutagenic Activity of Formaldehyde, when 18-hr. Larvæ are Treated for 24 hr.

Treatment medium	*sm*	*sm* + RNA (0·4 per cent) delayed	*sm* + RNA (0·4 per cent)
Formaldehyde concentration		$2 \cdot 0 \times 10^{-3}$ *M*	
Larval developmental time (days)	5·5	5·5	5·0
Per cent survivors	91·8	79·6	83·7
	First broods		
No. chromosomes examined	548	481	732
No. lethals	2	8	23
Per cent sex-linked recessive lethal mutations	0·36	1·66	3·14
	Second broods		
No. chromosomes examined	503	550	477
No. lethals	0	7	2
Per cent sex-linked recessive lethal mutations	0·00	1·27	0·42

survive if the ribonucleic acid concentration is less than 0·2 per cent or greater than 0·7 per cent.

While it was not possible to test the mutagenic activity of formaldehyde in the absence of ribonucleic acid, by treating larvæ throughout larval life, this difficulty was overcome after consideration of the following observations.

In a study of the response of *Drosophila* larval germ cells to the mutagenic activity of orally administered formaldehyde, Auerbach[5] has determined the patterns of sensitivity for each of the four days of larval life. In her initial experiments, larvæ were put on the formaldehyde food at the beginning of the stage to be treated, and transferred to ordinary food after 24 hr. It was afterwards discovered that, as formaldehyde food on which the larvæ are feeding loses its mutagenic activity within 24–48 hr.[5], transfer to ordinary food is not necessary; this means that approximately the same sensitivity pattern is obtained if the larvæ are allowed to complete development on the formaldehyde food as the ones transferred after only 24 hr. of treatment[5]. The ineffectiveness of formaldehyde food after 24–48 hr. does not appear to be due completely to loss of mutagenic activity of the medium[6], but rather to the development of a tolerance in treated larvæ which makes them incapable of responding to even a slightly deteriorated formaldehyde medium. However, if the larvæ which have spent some time on treated food are transferred to freshly treated food, formaldehyde can produce mutations in cells which would have failed to mutate with continued exposure to the old medium[7]. Observations on the sensitivity pattern of response of larval germ cells suggest the coincidence of the sensitive period with the auxocyte stage in primary spermatocyte development[5], that is, the protracted growth stage which precedes meiosis in the larval testis. Auxocytes are found to make their first appearance about the twelfth hour of the first day of larval life, which coincides with the beginning of sensitivity to formaldehyde food. Consequently, treatment of larvæ during the first day of larval life, whether the larvæ are allowed to complete development on the treatment medium, or are transferred to ordinary food after 24 hr., involves approximately the same effective treatment. In view of this latter consideration, it may be reasoned that the experiments quoted in Table 2 simply mean that, at the lowest concentration of ribonucleic acid (0·2 per cent), the appearance of the sensitive stage is delayed until the formaldehyde food has almost lost its effectiveness. This argument is unlikely, however, as the developmental time at 0·2 per cent ribonucleic acid is about the same as, and in one case (0·6 per cent) less than, for acid concentrations giving maximum mutagenic effect. Moreover, differences in speed of larval development do not necessarily result in altered mutational response to formaldehyde[7], although decreases in the mutagenic activity of formaldehyde have been reported after pronounced increases in the duration of larval life[7]. Nevertheless, it was decided to attempt to slow down development slightly on the synthetic treatment medium containing ribonucleic acid to obtain a comparable developmental time with the treatment medium where ribonucleic acid is omitted. This was achieved by halving the cholesterol concentration and substituting 0·004 per cent choline for the lecithin; these constituents were chosen as they have no known connexion with nucleic acid metabolism. Such a medium will be referred to as '*sm* + ribonucleic acid delayed'.

In consequence of the preceding observations, it was decided to pre-feed larvæ on *sm* + ribonucleic acid (0·4 per cent) medium for some time before transfer to the treatment medium, thus assuring that sensitive cells are present at the time of treatment. This procedure, however, has the disadvantage that a proportion of sensitive cells normally affected in the first brood will have passed the sensitive stage at the time of treatment; consequently, lower mutation rates occur.

Table 3 summarizes the results obtained when 18-hr. larvæ are treated for 24 hr., after which they are allowed to complete development on ordinary medium. In the absence of ribonucleic acid, no formaldehyde-induced mutagenic activity is detected; the spontaneous mutation-rate of the Oregon-*K* strain

Table 4. Effect of Ribonucleic Acid on the Mutagenic Activity of Formaldehyde, when 24-hr. Larvæ are Treated for 24 hr.

Treatment medium	*sm*	*sm* + RNA (0·4 per cent)	*sm* + RNA (0·4 per cent) delayed	*sm* + RNA (0·1 per cent)	*sm* + DNA (0·4 per cent)
Formaldehyde concentration			$2 \cdot 0 \times 10^{-3}$ *M*		
Larval developmental time (days)	5·5	5·0	5·5	5·5	5·5
Per cent survivors	61·8	62·6	55·4	70·6	64·6
		First broods			
No. chromosomes examined	579	602	605	599	582
No. lethals	2	21	12	1	0
Per cent sex-linked recessive lethal mutations	0·34	3·5	1·98	0·16	0·0
		Second broods			
No chromosomes examined	412	370	402	432	418
No. lethals	1	2	4	1	0
Per cent sex-linked recessive lethal mutations	0·24	0·54	1·0	0·23	0·0

Table 5. Effect of Ribonucleic Acid on the Mutagenic Activity of Formaldehyde, when 15-hr. Larvæ are Treated for 3 Days

Treatment medium	*sm*	*sm* + RNA (0·4 per cent)	*sm* + RNA (0·4 per cent) delayed
Formaldehyde concentration		$2{\cdot}0 \times 10^{-2}$ *M*	
Larval developmental time (days)	6·5	5·5	6·5
Per cent survivors	> 70	> 70	> 70
First broods			
No. chromosomes examined	603	501	557
No. lethals	0	28	21
Per cent sex-linked recessive lethal mutations	0·0	5·6	3·8
Second broods			
No. chromosomes examined	352	367	354
No. lethals	0	5	3
Per cent sex-linked recessive lethal mutations	0·0	1·36	0·85

varies normally from 0·1 to 0·3 per cent recessive sex-linked lethal mutations. In both acid series there is significant mutagenic activity, and although '*sm* + ribonucleic acid delayed' has the same developmental time as '*sm*', it shows no significantly different mutagenic response from '*sm* + ribonucleic acid' in either the first or second brood ($\chi^2 = 2{\cdot}5$ and $2{\cdot}14$, with one degree of freedom, respectively).

A comparable experiment where 24-hr. larvæ were treated by the same procedure is shown in Table 4. Again, no induced mutations are detected in the absence of ribonucleic acid, whereas activity is significant in both the '*sm* + ribonucleic acid' and '*sm* + ribonucleic acid delayed'; the mutational response of the latter two treatments do not differ significantly from one another in either the first or second brood ($\chi^2 = 2{\cdot}57$ and $0{\cdot}52$ with one degree of freedom, respectively). In this series, treatments were also carried out where the concentration of ribonucleic acid was reduced to 0·1 per cent (*sm* + ribonucleic acid (0·1 per cent)), and one where 0·4 per cent thymus gland deoxyribose nucleic acid replaces ribonucleic acid (*sm* + deoxyribonucleic acid (0·4 per cent)): no significant activity was detected after either treatment. Deoxyribonucleic acid was used here as it is known not to be utilized by *Drosophila* larvæ, and is even toxic to them[8]; at the concentration used here, however, the toxic effect is negligible.

Table 6. Effect of Ribonucleic Acid on the Mutagenic Activity of Formaldehyde, when 15-hr. Larvæ are Treated for 2 Days, and Re-treated on Fresh Formaldehyde Food for a further 2 Days

Treatment medium	*sm*	*sm* + RNA (0·4 per cent)	*sm* + RNA (0·4 per cent) delayed
Formaldehyde concentration		2×10^{-2} *M*	
Larval developmental time (days)	7·0	6·0	6·8
Per cent survivors	70·8	45·4	55·0
First broods			
No. chromosomes examined	744	640	668
No. lethals	2	16	22
Per cent lethals	0·27	2·5	3·3
Second broods			
No. chromosomes examined	355	362	337
No. lethals	1	7	6
Per cent sex-linked recessive lethal mutations	0·28	1·93	1·78

A further series (Table 5) is summarized, where 15-hr. larvæ were left on the treatment medium for three days, after which they were allowed to complete development on ordinary food. Once more, no induced mutations are detectable in the absence of ribonucleic acid, whereas '*sm* + ribonucleic acid' and '*sm* + ribonucleic acid delayed' both show high mutation-rates which are not significantly different from one another in either the first or second brood ($\chi^2 = 1{\cdot}98$ and $0{\cdot}43$ with one degree of freedom, respectively). The developmental times of '*sm*' and '*sm* + ribonucleic acid delayed' were almost identical, despite the increased duration of the treatment.

A final series was carried out, where advantage was taken of the fact that if larvæ, which have spent some time on formaldehyde-treated food, are transferred to freshly treated food, formaldehyde can produce mutations in cells which would have failed to mutate with continued exposure to the old medium[7]. Daily transfers to fresh formaldehyde food were carried out, but the effect on the development was found to be too pronounced except at low ($0{\cdot}5 \times 10^{-2}$ *M*) formaldehyde concentrations. However, less frequent transfers proved successful. Table 6 shows the results obtained when 15-hr. larvæ were left on formaldehyde food for two days, followed by transfer to fresh formaldehyde food for a further two days, after which they were allowed to complete development on ordinary food. No induced mutagenic activity was detectable in the absence of the acid, whereas both ribonucleic acid treatments showed mutagenic activity. The two acid treatments are not significantly different from one another in either the first or second brood ($\chi^2 = 0{\cdot}73$ and $0{\cdot}02$, with one degree of freedom, respectively); the developmental times of '*sm*' and '*sm* + ribonucleic acid delayed' were approximately the same.

Table 7. Effect of Ribonucleic Acid on the Mutagenic Activity of Urethane, when Treatment is for the Entire Larval Life

Treatment medium	*sm*	*sm* + RNA (0·4 per cent)
Urethane concentration	0·1 per cent	
Total developmental time	16–19 days	10–14 days
Per cent survivors	49	67·5
First broods		
No. chromosomes examined	964	648
No. lethals	14	10
Per cent sex-linked recessive lethal mutations	1·45	1·54
Second broods		
No. chromosomes examined	892	1,087
No. lethals	12	9
Per cent sex-linked recessive lethal mutations	1·34	0·83

That this phenomenon is not a general one for chemical mutagens is seen from Table 7, where I tested the mutagenic activity of urethane by the larval feeding method. Newly hatched larvæ were allowed to develop throughout larval life on the synthetic treatment medium under axenic conditions, and the mutagenic activity of urethane was tested in the presence and absence of ribonucleic acid; for both treatments urethane was autoclaved in the medium. Since urethane prolongs the pupal period, and adult emergence time is scattered over several days, developmental times are given from hatching from the egg to peak adult emergence. No difference was observed between the mutational response of the two series (first and second brood $\chi^2 = 0{\cdot}275$ and $1{\cdot}25$, respectively).

An analysis of the mechanism by which ribonucleic acid mediates the mutagenic activity of formaldehyde is now in preparation for publication.

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EFFECTS OF STARVATION ON THE ABILITY OF ISOLATED RAT DIAPHRAGM TO INCORPORATE LABELLED AMINO-ACIDS INTO ITS PROTEIN AND TO RESPOND TO THE INFLUENCE OF INSULIN ON THIS PROCESS

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IT is now well established that insulin *in vitro* stimulates the incorporation of labelled amino-acids into the protein of isolated rat diaphragm[1–4], although the mechanism by which this action is brought about remains unknown. The earlier experiments of Krahl[2] seemed to suggest that insulin enhanced incorporation of amino-acid into protein by favouring carbohydrate utilization, a process which would make available more energy and possibly more pentose for the synthesis of ribonucleic acid and protein. Addition of glucose to the medium, in place of insulin, could also simulate incorporation. More recently, both Manchester and Young[3] and Wool and Krahl[4] have described conditions under which addition of glucose has no observable effect on incorporation and yet where addition of insulin produces a very marked and consistent stimulation. However, Wool and Krahl[4] also find that a stimulating effect of glucose on incorporation of amino-acid can be observed with diaphragm from rats which have starved for 48 hr., the rate of incorporation in the absence of glucose being markedly depressed by comparison with diaphragm from the non-fasting animal. Under these conditions the effect of insulin on incorporation is very severely reduced. Similar results have not been obtained in this laboratory, and in the present communication evidence is presented to the effect that the nutritional status of the diaphragm donor (that is, the length of time, up to 48 hr., that the animal has starved before removal of the diaphragm) does not seriously modify the effect of insulin on incorporation, nor can the action of insulin on amino-acid incorporation be simulated in any way by glucose.

Diaphragm was obtained from female rats of either the albino Wistar or the black-and-white hooded strain, weighing about 120 gm. and fed a stock laboratory diet[5]. Diabetic animals had been rendered diabetic by subcutaneous injection of alloxan (200 mgm./kgm.) at least two weeks before removal of the diaphragm. Such animals had non-fasting blood sugar-levels above 500 mgm. per cent, but after the withdrawal of food for 24 hr. the blood sugar-level dropped to an average of about 215 mgm. per cent. Hemidiaphragms were incubated for 2 hr. at 37°C. in a bicarbonate buffer[7] *p*H 7·4, gassed with oxygen plus carbon dioxide (95 : 5) in the presence of 1–^{14}C–glycine (1 μmole/ml.), with or without addition of glucose (2·5 mgm./ml.) and/or insulin (Boots crystalline insulin – 22 units/mgm., 0·1 unit/ml.). The procedure for the removal and incubation of the diaphragm and for the preparation of protein samples has been previously described[3]. In the experiments with diaphragm from Wistar rats the glycine added to the medium had a specific activity of about 400 μc./m.mole; the protein prepared from diaphragms was collected on 1-cm.^{2} plastic disks as infinitely thick samples[6]. In the experiments with diaphragm from the hooded rats the glycine added to the medium had a specific activity of about 80 μc./m.mole; the diaphragm protein was collected as a thin film on 7·5 cm.^{2} aluminium disks, and its content of radioactivity assessed in counting equipment with an efficiency for carbon-14 of about three times that of the equipment used for counting the infinitely thick protein samples. The figures shown for incorporation of radioactivity into protein of diaphragm from the two strains of rat are therefore not comparable. Other experiments in which the rate of incorporation by diaphragm of the two strains has been compared suggest that the respective rates are fairly similar.

In the absence of insulin, incorporation of ^{14}C-glycine into the protein of diaphragm from Wistar and hooded rats starved 24 hr. was slightly (13 and 12 per cent) reduced by comparison with diaphragm from non-fasting animals (Table 1). A further 24 hr. of starvation did not appreciably reduce incorporation in either strain. In the presence of insulin, incorporation into protein of diaphragm from Wistar rats starved for 24 hr. had declined 10 per cent by comparison with diaphragm from non-fasting animals, but incorporation did not decline further when the diaphragm donors starved for 48 hr. (Table 1). Starving hooded animals for 24 hr. did not depress the rate of incorporation of glycine by the isolated diaphragm in the presence of insulin, though with diaphragm from rats starved for 48 hr., incorporation was appreciably (21 per cent) lower (Table 1). With diaphragm from the Wistar rats the magnitude of the effect of insulin on incorporation of ^{14}C-glycine was unchanged by the nutritional pre-treatment of the diaphragm donor, and was about four times the size of the change induced by starvation (Table 1). With

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Table 1. Effect of Fasting on the Incorporation of ^{14}C-glycine into the Protein of Isolated Rat Diaphragm and the Stimulation by Insulin of this Process

Strain of rat from which diaphragm taken	Food withheld (hr.)	Radioactivity in diaphragm protein		
		No insulin added	Insulin added (0·1 unit/ml.)	Difference
		(counts/min./disk)		
Wistar	0	281 ± 15	442 ± 19	161
	24	242 ± 14 } $P < 0·1$	406 ± 17	164
	48	250 ± 9	401 ± 16	151
		(counts/min./mgm.)		
Hooded	0	11·9 ± 0·94	18·0 ± 1·22	6·1
	24	10·4 ± 0·88 } $P < 0·1$	17·6 ± 1·56 } $P < 0·05$	7·2
	48	9·8 ± 0·62	14·2 ± 0·85 } $P < 0·1$	4·4

Each figure is the mean ± S.E. of the mean of six observations. The value of P for a difference which is significant is indicated. The effect of insulin is significant in each instance ($P < 0·01$). No glucose was added to the medium.

diaphragm from the hooded strain the size of the insulin effect was somewhat reduced when the donor had starved for 48 hr., though this diminution was not apparent with diaphragm from rats starved for 24 hr. (Table 1). The magnitude of the insulin effect, however, was still twice the diminution in incorporation produced by starvation.

Addition of glucose or pyruvate to the medium in either the presence or absence of insulin has previously been shown to have no observable effect on the incorporation of a large number of different ^{14}C-labelled amino-acids into the protein of diaphragm from Wistar rats starved for 20–24 hr.[2]. Addition of glucose to the incubation medium, again in the presence or absence of insulin, has now been found to have no appreciable or significant effect on the incorporation of ^{14}C-glycine into the protein of diaphragm from rats of either strain starved for 48 hr. or from alloxan-diabetic Wistar rats starved for 24 hr. (Table 2). The magnitude of the insulin effect is also unchanged by the addition of glucose, and is many times larger than any effect of glucose.

Since Wool and Krahl[4] were using rats of the Sprague-Dawley strain, the results presented here may indicate that there are quite large quantitative differences in the response of different strains to the effects of starvation, glucose and insulin on amino-acid incorporation. In particular, rats of the Sprague-Dawley strain, as judged by the ability of the isolated diaphragm to incorporate labelled amino-acids into protein, appear to be incapacitated to a greater extent by starvation than are those of the Wistar and hooded strains. In other words, availability of the energy required for protein synthesis becomes a rate-limiting factor at an earlier stage during starvation in the Sprague-Dawley rat. Perhaps because of this an enhancement of the rate of amino-acid incorporation by addition of glucose is more readily observed with the isolated diaphragm of this strain[5]. On the other hand, slight variations in the conditions under which the animals are reared and kept may lead to quite large differences in the response of diaphragm to the conditions investigated.

The results presented here, taken in conjunction with earlier papers from this laboratory[2,3], do indicate, perhaps more clearly than hitherto, that insulin *in vitro* invariably stimulates incorporation of labelled amino-acids into the protein of isolated diaphragm from rats in varied nutritional states, and that this effect of insulin is not dependent upon an effect of insulin on glucose uptake, neither can it be simulated by glucose alone, nor is it observably modified by the simultaneous presence of glucose. The availability of material acting as a source of energy for protein synthesis, even for the alloxan-diabetic animal, is not therefore the rate-limiting step in amino-acid incorporation in diaphragm, and the action of insulin on this process does not appear to be brought about by its action on carbohydrate metabolism. The slightly reduced basal incorporation observed here which results from starvation for 24 or 48 hr. may be a consequence of a reduced rate of secretion and lower circulating level of insulin than is the case in the non-fasting animal.

Although insulin enhances the rate of accumulation of a non-utilizable amino-acid, α-amino isobutyric acid, by diaphragm[10], it has not so far proved possible to show an effect of insulin on the accumulation of naturally occurring amino-acids in the same way[11]. The bulk of the evidence at the present time[11–13] is against the view that insulin enhances amino-acid incorporation into muscle protein by affecting the transfer of amino-acids into the cell, but the details of the mechanism by which insulin regulates amino-

Table 2. Effect of the Addition of Glucose to the Medium on the Incorporation of ^{14}C-glycine into the Protein of Diaphragm from Fasting Rats and the Stimulation by Insulin of this Process

Food withheld (hr.)	Strain of rat from which diaphragm taken	Addition to the medium	Radioactivity in diaphragm protein		
			No insulin added	Insulin added (0·1 unit/ml.)	Difference
				(counts/min./disk)	
48	Wistar	No addition	187 ± 8*	317 ± 11	130
		Glucose (2·5 mgm./ml.)	208 ± 9	312 ± 14	104
				(counts/min./mgm.)	
48	Hooded	No addition	10·7 ± 0·68	16·7 ± 1·29	6·0
		Glucose (2·5 mgm./ml.)	11·7 ± 0·81	17·5 ± 0·82	5·8
				(counts/min./disk)	
24	Alloxan-diabetic Wistar	No addition	200 ± 14*	337 ± 23	137
		Glucose (2·5 mgm./ml.)	203 ± 11	338 ± 21	135

Each figure is the mean ± S.E. of the mean of six observations. The effect of the addition of glucose is in no case significant. The effect of insulin is significant in each instance ($P < 0·01$).

* These figures cannot be compared, as the experiments were performed at different times with different batches of ^{14}C-glycine in which the content of radioactivity had not been rigidly standardized.

acid incorporation and protein synthesis remain obscure.

I am grateful to Prof. F. G. Young for much help and encouragement during the performance of this work.

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A HEPATOTOXIN CAUSING LIVER DAMAGE IN FACIAL ECZEMA OF SHEEP

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FACIAL eczema is a serious disease affecting sheep and cattle in many areas in New Zealand. The disease is essentially an acute cholangitis which, in more severe cases, is accompanied by obliteration of medium-size bile ducts, with bile ductule proliferation, and a gradual replacement of liver parenchyma in the portal areas with fibrous tissue as the lesions become more extensive[1]. It has recently been shown that this condition is due to a toxic principle present in the fungus *Sporidesmium bakeri*, Syd., a saprophytic organism growing in association with pasture[2]. Rabbits and guinea pigs are also known to be susceptible to the disease, liver lesions of a generally similar nature having been demonstrated in these species after feeding toxic grass and pure fungal culture[3,4], and ether extracts of these[4], and also after the injection of extracts into the vena porta[5].

Little is known of the behaviour of the toxin in the animal body. It has been generally assumed that the toxin is transported via the portal circulation to the liver and excreted into the biliary system, where it sets up an inflammatory reaction which in turn produces lesions characteristic of the disease[6]. There is, however, no experimental evidence to substantiate that the portal circulation is the main route by which the toxin enters the liver, nor is there any direct proof of the presence of the toxin or of a possible metabolite in the bile. These problems have recently been studied in some detail at this Station.

Transport of Toxin to the Liver

In an attempt to confirm the portal route of entry into the liver, and in order to obtain information on the rate of uptake of the toxin from the circulation, a comparison of the effectiveness of fungal extracts administered by the portal vein and by the jugular vein was made. A range of doses was tested on New Zealand white rabbits of mixed sex weighing 1,000–1,200 gm. Twelve animals were allotted to each group at random. All animals were slaughtered eight days after treatment. Morbid anatomy and histological examinations of specimens taken *post mortem* were carried out by D. C. Dodd, veterinary diagnostic officer, of this Station.

It has been found that over wide levels of dosage (ranging from the equivalent of 300 ml. to 1,000 ml. of fungal culture), macroscopic lesions of varying severity, consistent with facial eczema liver damage, were produced after intraportal injection of toxic extracts (Figs. 1, 2). The extent and severity of these

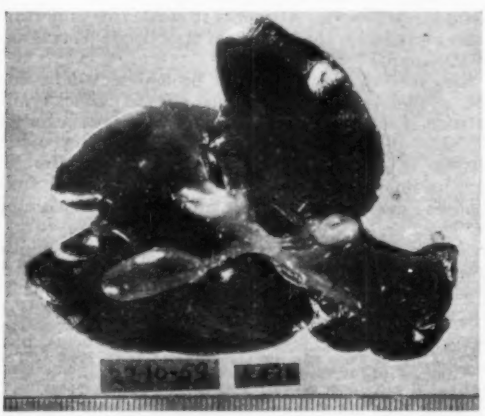

Fig. 1. Severe liver damage in rabbit fed a culture of *Sporidesmium bakeri*, Syd. for 14 days. Note extreme œdema of hepatic ducts, common bile duct and cystic duct, and marked fibrosis of left central lobe. Scale in millimetres

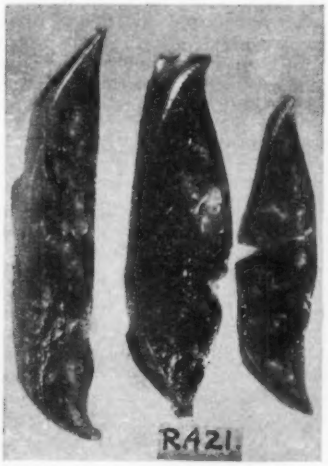

Fig. 2. Transverse sections of liver from same rabbit illustrating generalized damage to duct system

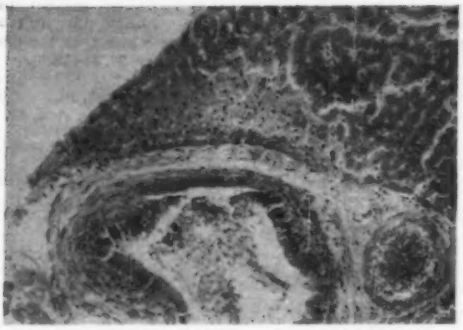

Fig. 3. Photomicrograph of local necrosis and desquamation of biliary epithelium of large bile duct with moderate periductal œdema and fibrosis. Hæmatoxylin and eosin. (×70)

lesions were confirmed histologically (Figs. 3, 4). After injection of comparable amounts of toxic material into the jugular vein, on the other hand, no evidence of any gross liver damage was found, and all livers, with the exception of two, were histologically normal. The two positive livers were graded as 'mild' on histological examination.

These observations provide support for the hypothesis that the portal circulation is the main route by which toxin enters the liver following absorption from the intestinal tract. The evidence also indicates that the toxin is relatively unstable in the systemic circulation and, on the basis of these findings, it would appear that uptake of toxin via the lymphatic system is of little or no importance in so far as the development of liver lesions is concerned. The fact that the toxin appears to be inactivated on entering the general circulation would suggest also that the uptake of toxin by the liver cells is instantaneous and that the lesions produced must, therefore, be due to that fraction of the toxin removed from the portal blood the first time it passes through the liver sinusoids.

Appearance of Toxin in the Bile

Prior to the work reported here, it had already been shown, in independent studies, that the first bile duct lesions begin to appear approximately three to six hours after intraportal injection of toxic extract[5], which strongly suggested that if toxin is excreted into the bile it must reach relatively high concentrations there very shortly after injection. It was decided, therefore, to collect bile from animals for varying intervals following injection of toxic extract and to test this bile directly for toxicity. Rabbits, of mixed sex, weighing 600–1,000 gm. were used. 'Donor' animals were fitted with a cannula into the common bile duct and injected intraportally with toxic extract equivalent to 5 litres of fungal culture. Toxicity was assessed by dripping the bile from the donor into the top of the duodenum of successive 'recipient' animals, up to six recipient animals being used in each experiment. This technique was decided upon after it had been shown independently that toxic extracts dispersed in fresh hepatic bile and administered in this way were effective in producing typical lesions of severe facial eczema liver. The technique offered the further advantage of minimizing the time for which any toxin present would be in contact with bile and also avoided the necessity for any form of chemical or physical treatment of the bile, which would have been necessary in order to reduce its bulk were it to be administered by any other route.

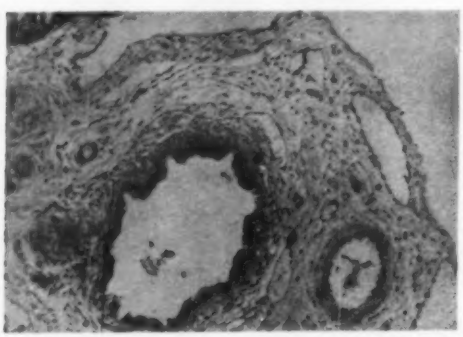

Fig. 4. Photomicrograph demonstrating typical severe periductal œdema and fibrosis, and cellular infiltration of periductal tissue. Hæmatoxylin and eosin. (× 70)

Fourteen such experiments have been carried out to date. The technique employed in each has been essentially the same, with the exception that the intervals over which individual recipient animals received bile from the donor animal were varied in the different experiments from half an hour up to one and a half hours, although within each experiment the intervals were kept constant. In eleven of the fourteen experiments the presence of toxic material in the bile of the donor animal has been unequivocally demonstrated by the development of typical liver lesions of facial eczema in the recipient animals. The negative results obtained in three experiments were believed to be due to loss of toxicity of fungal extract prior to injection into the donor. In view of the wide individual variation in the degree of liver damage between animals which was observed in each experiment, it is difficult to assess with any degree of accuracy the rate of excretion of toxin from the liver. The evidence obtained so far does clearly indicate, however, that appreciable amounts of toxic material are present in the bile in as little as half an hour after injection of extract, and that maximal output appears to occur within two hours of injection. Whether the observed toxicity of bile was due to the presence of the toxin *per se* or to physiologically active degradation products of the toxin is not known. Attempts to settle this important issue must await elucidation of the chemical structure of the toxin.

The fact that toxicity has been detected in bile, using the technique outlined, is of considerable interest for our understanding of the pathogenesis of this disease, since it quite clearly provides strong evidence for supposing that in the intact animal an enterohepatic circulation of toxic material may occur. This might assist in explaining, at least in part, the 'progressive' nature of the disease[1], and the fact that such seemingly minute traces of toxin are capable of producing, in many cases, lesions of the most severe form (White, E. P., unpublished work).

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LETTERS TO THE EDITORS

PHYSICS

Copper-Cellulose Complexes

THE criticism recently levelled by Bayley and Rose[1] at our findings concerning a copper–cellulose complex in wood implies that they have neither appreciated the weight of our evidence nor have they realized the complexity of the problems involved. We recommend that they should see all our papers on this matter[2–6]. We are answering these criticisms on behalf of the authors involved in our papers as we were responsible for the physical evidence presented.

When copper is taken up by wood and complexes in such a way as to be detectable by our methods, the question is whether the particular complex concerned is associated with the cellulose on one hand (as we believe we have proved), or with the encrusting substances (as Bayley and Rose would have us believe) on the other. This latter possibility must be rejected on several clear grounds. (*a*) The complex gives identically the same electron diffraction patterns whether whole wood or wood α-cellulose is used and, moreover, these are invariable for a wide range of α-celluloses and a wide range of metals. (*b*) The complex is oriented with respect to the cellulose microfibrils. This is demonstrated both by the electron diffraction diagram and by the dichroic properties resulting when wood or α-cellulose is treated with a copper salt and stained with dithioxamide. There is no evidence that the encrusting substances have the requisite properties. (*c*) The uptake/concentration curves demand that the copper shall be adsorbed on a surface, and the electron diffraction diagrams prove that the copper ions then form a regular two-dimensional array. The microfibrils provide such a regular surface, but there is no evidence that the encrusting substances fulfil this requirement.

We have emphasized in our papers that copper, in particular, occurs in more than one form in wood impregnated with copper salts and of course it may form a complex with some of the encrusting materials. We have been careful not to exclude this possibility though we have at present no evidence for it; our evidence refers exclusively to a copper–microfibril complex. It is not quite certain that the complex involves any part of the glucose residue in cellulose, and non-glucose sugars that are known[7] to be an integral part of the cellulose microfibril may be involved. The facts, however, that the same electron diffraction diagram is obtained for celluloses varying widely in xylose content, and that if non-glucose sugars are involved they would need to be closely and regularly distributed over the surface of microfibrils, argue strongly in favour of glucose. For the same reasons we are of the opinion that the hydroxyl groups of glucose are involved rather than occasional carboxyl substituents.

It is perhaps at first sight peculiar that microfibrils embedded in lignin and hemicelluloses possess the necessary free surfaces, and it is presumably this that formed the starting point of Bayley and Rose's[1] comments. It must be remembered, however, that by no means all of the microfibrils either in wood or in wood α-cellulose become complexed. The evidence so far is that less than about a quarter of the total microfibrillar surface is apparently capable of adsorbing metals in the manner under consideration. The evidence shows that this much of the surface is available in wood, and unless our evidence can be shown to be at fault this must be accepted.

We would suggest that, until firm evidence to the contrary has been presented, our hypothesis is the only reasonable interpretation of the facts.

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Sorption of Activated Gases by Titanium Films

GALE[1] has shown that the rate of gas sorption of an evaporated titanium film is enhanced by a Penning gauge connected to the getter vessel, and experiments are in progress in my laboratory to determine the nature of the sorption process when the gas is activated in this manner. In a recent communication it has been shown that the rate of gas sorption of titanium films for air, nitrogen, oxygen and hydrogen are a function of the current flowing in the Penning head[2], even when the metal film is at a positive potential and therefore repels positive ions. The increase in the rate of sorption of active gases greatly exceeds that due to the pumping action of the Penning head, but inert gas atoms are only sorbed by the Penning head and are probably embedded in metal sputtered from the cold cathodes.

I have proposed[2] that the enhanced rate of sorption of an active gas arises primarily from the Penning discharge atomizing the gas, so that it diffuses more readily between the grain boundaries of the metal deposit. Possibly the active states of the gas particles also increase their rate of chemical reaction at the nascent metal surface; but this can scarcely explain an enhanced rate of sorption if one considers that sorption proceeds through a superficial layer of reaction products. Titanium films evaporated at low pressure ($< 0{\cdot}1\mu$ mercury) have almost bulk density, because when oxidized by heat the resulting layer of titanium oxide has a refractive index near that of solid rutile in the polycrystalline state. Evaporated titanium films grow from a large number of nuclei, and the condensate must be composed of tightly packed micro-crystallites possessing a large interior

area for adsorption and reaction with residual gases. However, the rate of sorption of a fresh film would rapidly decline, because the gas molecules are unable to reach the interior surface. Dependence of the rate of diffusion of the sorbed gas on the structural form of the deposit may account for the conflicting reports of the effects of ionization (or atomization) of gases on the rate of sorption of barium (see, for example, refs. 3 and 4), because with this metal the grain size and distribution can vary considerably with the evaporation conditions.

The investigations of the gettering properties of titanium have recently been refined and show more clearly the dependence of the rate of sorption on the ionization (atomization) of the residual gas. The Penning ion-source was mounted in a 3-in. diameter tube with titanium cathodes of 3 in. diameter and in a magnetic field-strength of 400 gauss. When operated at applied voltages between 3 and 5 kV., the ion-source had a pumping speed of about 1–5 litre/sec. The sorption vessel consisted of a stainless steel chamber 6 in. in diameter and 6 in. high (1,400 cm.^{2} area) with the Penning head mounted on top. The positive terminal of the high-tension supply was grounded, so that the evaporated getter repelled gas ions. The vacuum seals were made with metal gaskets and the pressure measured with an Alpert type ion-gauge. The titanium was evaporated from tungsten filaments after baking the system and isolating the chamber from the oil diffusion pump at a pressure of 10^{-7} mm. mercury. The gas to be sorbed was admitted to the getter chamber from a reservoir through a calibrated leak. Rates of sorption were measured in the pressure interval 10^{-7} to 10^{-5} mm. mercury.

In the earlier work[1], a thick titanium film was used for a series of sorption measurements over a range of pressures. In this investigation a fresh film ($\simeq$ 100 Å. thick) was used for each sorption measurement, and a period of 1 min. was allowed after each evaporation for the system to gain equilibrium before the instantaneous rate of sorption was measured. At the pressures used, the outer surface of the getter film was rapidly covered by adsorbed gas, and this was shown by the fact that the rate of sorption fell to a negligible amount ($< 0{\cdot}002$ litre μ/sec.) after a few minutes if the Penning head was not on. In Fig. 1 are shown the mass sorption-rates of titanium films for oxygen when measured at different pressures and under the foregoing conditions. The Penning head was operated at constant voltages of 3 and 5 kV., and the current flowing in the head has been plotted in Fig. 1 as a function of pressure. When the two sets of curves are compared, it can be seen that the rate of sorption is practically a linear function of the Penning discharge current, which itself is not exactly proportional to pressure. At high values of ionization current the rate of sorption tends to increase less rapidly, presumably because the getter film is more quickly saturated by the gas.

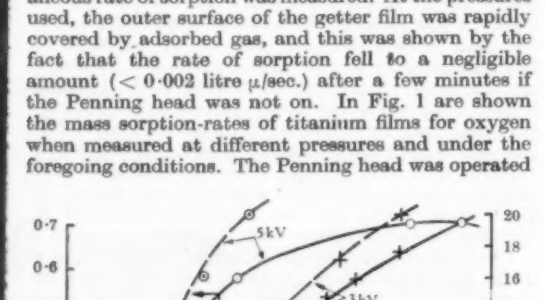

Fig. 1. Dependence of the sorption-rate of titanium film for oxygen on the current flowing in the Penning head

In a recent communication in *Nature*, Stow[5] reported that titanium films deposited on the negative ion collector of a hot-cathode ion-pump gave the same rate of sorption whether the ion-pump was in operation or not. From this he concluded that ionization did not play an essential part in the sorption process. However, his pressure measurements were made with a Penning gauge and if, as suggested here, such a discharge supplies atomized neutral particles to the film, then operation of the gauge would have enhanced the rate of sorption in both cases. The ionization (and related dissociation) efficiency of a Penning system is known to be superior to that of a triode type ion-source. These criticisms do not in any way detract from his substantiation of the value of titanium as a getter. Stow's subsequent experiments comparing barium and titanium getters were based on measurements made with Alpert ion-gauges, and molecular dissociation could have still been effective.

The theory advanced in this communication to explain the enhanced rate of sorption of a deposit also accounts for the enhanced rate of oxidation of thin metal films in glow discharges. There is no evidence that oxide films on metals grow faster in the presence of active oxygen, but penetration of a metal film by gas atoms so that the crystallites are oxidized on many sides would explain this phenomenon.

Acknowledgments are made to Mr. W. Sheraton, who made the sorption measurements described here, and to the Directors of Edwards High Vacuum, Ltd., for permission to publish this communication.

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Sedimentation and Effective Viscosity

I wish to comment on the communication by Prof. G. J. Kynch on this subject[1]. With the author's reservations (see following letter), the derivation of equation (8) seems satisfactory, though it is difficult to see the need for the constant added in equation (6). The final equation may be written in the form :

$$V_r = \frac{u}{V} = \frac{(1 - c)}{\mu_{re}} \qquad (1)$$

where V_r is relative settling velocity of particles ; u is actual settling velocity of particles ; V is settling velocity of a single typical particle at infinite dilution

c is volume concentration of solids; μ_{re} is effective relative viscosity of suspension of similar particles having the same density as the fluid and a volume concentration of c. This equation makes interesting comparison with equations due to Gurel[2],

$$V_r = \frac{(1-c)^2}{\mu_r} \qquad (2)$$

where μ_r is the measured relative viscosity of the suspension, and Hawksley[3],

$$V_r = (1-c)^2 \exp - \frac{2{\cdot}5c}{1 - 0{\cdot}609c} \qquad (3)$$

and Steinour[4],

$$V_r = (1-c)^2\, 10^{-1{\cdot}82c} \qquad (4)$$

All four equations contain a term which represents the reciprocal of the effective relative viscosity of the suspension; this is multiplied by $(1-c)^2$ in equations (2), (3) and (4), and by $(1-c)$ in equation (1). The latter term is due to the familiar 'return flow' effect, also considered by the other workers; the additional factor $(1-c)$ in equations (2), (3) and (4) appears because a typical particle is considered as settling in a fluid of density equal to that of the suspension as a whole rather than one of density equal to that of the dispersing liquid. Kynch, however, considers a typical particle differing from its fellows only in that its density is equal to that of the dispersing liquid. The time-average velocity of this particle is stated to equal the mean fluid velocity "modified by the pressure gradient in the fluid due to the [other] falling particles". Following the application of an equation in which the density of the particle reverts to its original value, a value of the settling velocity is obtained by neglecting the above pressure gradient. Equation (1) is therefore advanced only as an 'approximate' relationship for the settling velocity.

It is then stated that the equation "seems to agree with experimental results up to concentrations of about 20 per cent", ref. 5 being quoted. This agreement is actually rather poor, for the curve referred to shows that the product $\mu_r V_r$ is proportional to $(1-c)^2$ rather than $(1-c)$; thus distinct non-linearity is present at concentrations of less than 20 per cent when the data are plotted on the basis of $\mu_r V_r$ against $(1-c)$. Moreover, in the derivation of equation (1), it was stated that the viscosity was that of an otherwise similar suspension in which the particles had the same density as the fluid, that is, a stable suspension. Accordingly, a graph has been drawn in which the relative viscosities used are for stable suspensions of spherical particles[6] and the settling velocities for otherwise similar slightly unstable suspensions having particle size ratios of 1·40 : 1 (ref. 7) and 1·03 : 1 (ref. 2), respectively (Fig. 1). In neither case does equation (1) apply satisfactorily, although for the suspensions having particles of wider size-range the gradient of the line near the origin is not greatly different from that predicted by the theory. The suspensions of closely sized particles represent an important limiting case on which few data are available; the unique settling behaviour of these suspensions merits further attention.

It should be added in fairness that equation (2) also requires modification before agreement with experimental results is obtained[5]. Fair agreement with the present data has, however, been given by equation (3), linear plots being obtainable for concentrations up to more than 30 per cent with gradients

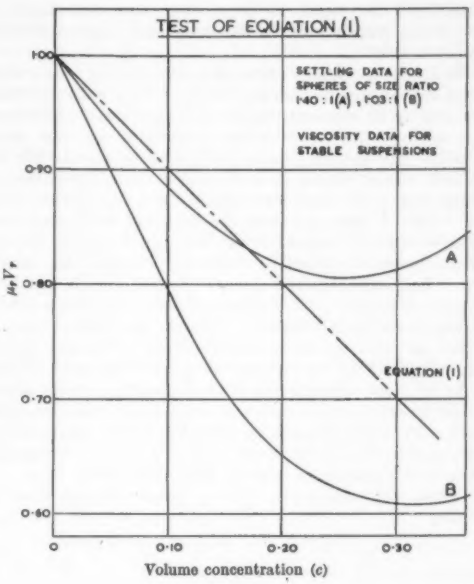

Fig. 1

of 1·26 (size ratio 1·03 : 1) and 0·88 (size ratio 1·40 : 1), compared with a theoretical value of 1·09. These figures illustrate the importance of reducing the size-range of particles used in sedimentation tests if the results are to be compared with elementary theory.

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Before I comment on Dr. Oliver's communication, I feel that an apology is due to readers for a number of errors in my communication in *Nature* of October 24. They made a simple derivation of equation (8) appear complicated though not, I hope, unintelligible.

Dr. Oliver's comments are valuable, as he is familiar with the difficulties of this subject, and I am glad that he considers that the derivation of my equation seems satisfactory and produces no theoretical reasons for disagreeing with it. Incidentally, the other equations which he mentions are referred to and commented upon by Ward in the reference given in my letter.

At present the experimental results on suspensions seem complicated and often have surprising features. Objections can be raised to all theoretical formulæ or semi-empirical formulæ yet suggested, and the reasons for the complications are not fully understood. In these circumstances, as in many others, the most useful theory is simple, generally acceptable, containing well-defined approximations with some physical meaning. It may then be possible to suggest reasons for discrepancies between the approximate theory and accurate experiment which will lead to an

improved formula. I hope that the derivation in my letter might help in this way and suggest further experiments.

Dr. Oliver clearly does not accept my statement that my equation "seems to agree with experimental results up to concentrations of 20 per cent", although he admits that the other equations are not good either. He mentions my reference to the article by Ward, where there is certainly a curve intended to show that $\mu_r V_r$ is proportional to $(1 - c)^3$ rather than $(1 - c)$. I was not entirely satisfied with this conclusion and I looked at the data used in the article, which were obtained by Oliver[2]. In fact, his results for 'Kallodoc' spheres in water and in an alcohol–water mixture and for glass spheres in glycerol–water agree quite well with my formula, as I stated, and at least as well as with the formula with the factor $(1 - c)^3$. Only for 'Kallodoc' spheres in lead–nitrate solution was there serious error and for suspensions with nearly equi-sized particles. Dr. Oliver plots two curves using viscosity data for stable suspensions, one giving fair agreement and the other, for nearly equi-sized particles, giving bad agreement.

From my equations (1)–(4), which I reproduce in order :

$$v = v_f + v_p : \quad U = v' - v : \quad U\mu = V\mu_0 : \quad v' = u$$

together with the assumption $v_f = -cu/(1 - c)$, I deduce that :

$$\mu u = (1 - c)(\mu_0 V + \mu v_p)$$

The discrepancies in my simple formula can be attributed to its assumption that $v_p = 0$, or to the other assumption that μ is the effective viscosity μ_{re}.

Whatever the cause, the discrepancy for equi-sized spheres is puzzling and requires more consideration.

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METALLURGY

Influence of Guinier–Preston Zones on the Electrical Resistivity of Age-hardening Alloys

Federighi and Passari[1] have recently directed attention to the increase in electrical resistivity associated with the early stages of ageing in binary aluminium alloys in which age-hardening involves pre-precipitation effects such as the formation of Guinier–Preston zones. Recent work in this Establishment has shown that this effect occurs in more complex ternary and quaternary aluminium alloys and is particularly marked in the Al–Zn–Mg–Cu system.

The effect is shown in Fig. 1, which compares present observations on an Al–Zn–Mg alloy with earlier work by Durer and Köster[2]. Ageing at 20° C. yields a significant increase in resistivity whereas at high temperatures the normal fall in resistivity associated with precipitation is observed. Very similar results have now been obtained on commercial Al–Mg–Si alloys (Fig. 2) and the effect appears to be typical of a number of binary and ternary aluminium alloys, including duralumin type alloys[3], all of which are known to develop Guinier–Preston zones in the initial stages of hardening and particularly during

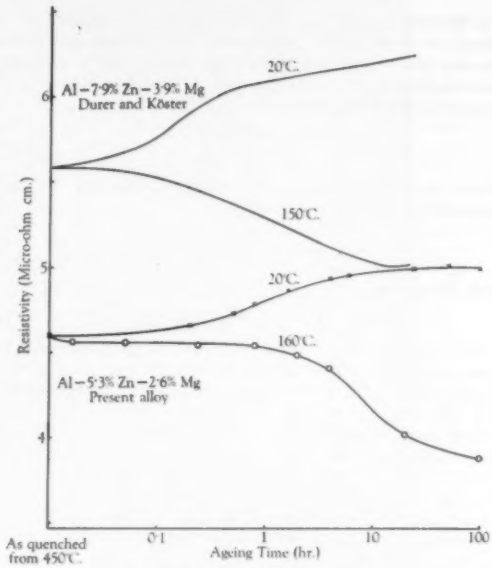

Fig. 1. Isothermal ageing Al–Zn–Mg alloys

low-temperature ageing. The lack of coincidence between the resistivity and hardness increases has been ascribed to the dependence of the resistivity on electron scattering by aggregates of criticial dimensions and on the effect of coherency strains in the matrix[4,5]. In the Al–Zn–Mg system it is known that low-temperature ageing involves the segregation of Zn–Mg zones coherent with the matrix which develop to dimensions of the order of 25 Å. × 50 Å. diameter, followed by the development of an intermediate, hexagonal precipitate which gradually loses coherency with the matrix. However, Guinier–Preston zone formation undoubtedly occurs in the early stages of high-temperature ageing as well, for such zones are readily developed during quenching and heating to the ageing temperature. If the above hypothesis is correct then the loss of resistivity in the early stages of high-temperature ageing must be ascribed to accelerated growth of the zones beyond critical dimensions and earlier development of intermediate precipitates which are not markedly coherent with the matrix.

Fig. 3 shows the profound effect of adding copper to an Al–Zn–Mg alloy of similar composition to that in Fig. 1. The ageing process is retarded and the resistivity changes are far more marked and persist to higher ageing temperatures. Single-crystal X-ray work on these alloys has shown that the Guinier–Preston

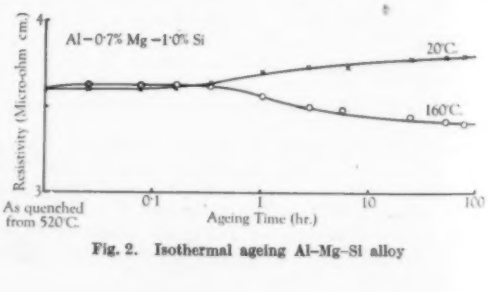

Fig. 2. Isothermal ageing Al–Mg–Si alloy

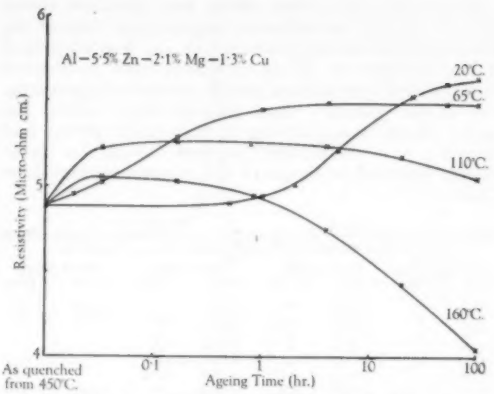

Fig. 3. Isothermal ageing Al–Zn–Mg–Cu alloy

zone structure once established is particularly stable and persists even during ageing at 160° C. and higher. The experimental evidence suggests that ideally the zone structure would not develop at ageing temperatures above 110° C., but in practice does so during heating to the ageing temperature (heating time less than 1 min.). For ageing temperatures of 110° C. and above the resistivity changes and mechanical properties of this alloy are significantly affected by the rate of heating to temperature, both peak hardness and peak resistivity being increased by slow heating.

For these higher ageing temperatures the resistivity peak is closely associated with the primary hardness increase, and it is reasonable to suppose that the resistivity effect is more closely associated with high coherency strains rather than with the existence of zones of critical dimensions. Thomas and Nutting[6] estimate that the zone diameter in this quaternary material is of the order of 80 Å.

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Purification of Metals by Gas Chromatography

The use of chromatographic techniques for the separation of an alloy into its constituent elements or for the direct purification of metallic elements has not, to our knowledge, been reported. In order to test the feasibility of the separation a zinc–cadmium (8·4 per cent zinc) alloy was used. The advantages of this alloy system for this test are: (1) both elements have significant vapour pressures at temperatures which do not pose extremely difficult material problems; (2) they are chemically similar; (3) they are common metals; (4) their reactivity is small enough so that they pose no handling problems (as would the alkali metals).

The containing tube was a 50-cm. length of 13-mm. 'Vycor'. The stationary phase, lithium chloride, was supported as a film on sea sand (20 per cent lithium chloride, 80 per cent fine sea sand). The temperature was high enough so that the lithium chloride melted and formed a film on the sand. The eluting gas, purified helium, had a velocity of 150 ml./min. and was preheated to 620° C., the bed temperature. The 0·1-gm. sample of alloy was laid on top of the bed before heating. It was necessary to eliminate most of the oxygen and water from the system in order to minimize oxidation of the sample. The emerging metal vapours were caught on glass cold fingers held in the gas stream for a short time. The metal was dissolved in distilled nitric acid and analysed spectrographically.

It was shown that the cadmium content of the vapour was more than 200 times the zinc content. The amount of zinc present was near the lower limit of the analytical procedure. It was also shown, by duplicating the above experiment without the stationary or solid phases, that the process was not that of simple distillation. In this case the zinc deposit was equal to, or greater than, the cadmium deposit. Although neither of the constituents was collected quantitatively, these experiments suggest that metals can be efficiently separated.

I wish to acknowledge the assistance of Messrs. S. Greenberg and C. A. Youngdahl. This work was done under the auspices of the U.S. Atomic Energy Commission.

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CHEMISTRY

Decomposition of Uranium Dioxide at its Melting Point

We have found that fusion of uranium dioxide in an argon arc furnace at 2,800 ± 100° C., between a tungsten cathode and a water-cooled copper anode, consistently gave lustrous grey metallic-looking products, with the gross analytical composition UO_{3-x} $(0{\cdot}15 > x > 0)$. The fused material was contaminated with less than 0·001 per cent of copper or tungsten. The extent to which the product was deficient in oxygen depended upon how long the sample had been held in the molten state, but the liquid seemed to approach a limiting composition, about $UO_{1\cdot86}$, after prolonged fusion. There was some vaporization from the melt, but the constitution of the vapour phase is unknown; after exposure to air, the powdery sublimate present in the furnace consisted of the oxygen-excess phase UO_{2+x}.

The massive fused material was quite stable in air, but when it was powdered it readily combined with oxygen, up to a composition around $UO_{2\cdot005}$. X-ray analysis of a fine chip of the fused product revealed the presence of two phases.

(*A*) The major phase (estimated 94–98 mole per cent) was face centred cubic with $a_0 = 5{\cdot}4718 \pm 0{\cdot}0004$ Å., which may be compared with the fluorite cell of essentially stoichiometric uranium dioxide, $UO_{1\cdot000 \pm 0\cdot001}$, with $a_0 = 5{\cdot}4700 \pm 0{\cdot}0004$ Å.

This small but significant expansion of the uranium dioxide lattice, which has also been observed when uranium metal and uranium dioxide are heated above 2,000° C. in a graphite resistance furnace[1], is taken to

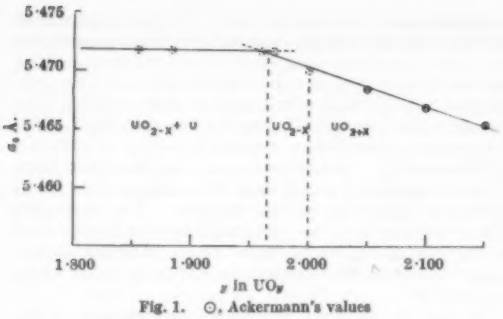

Fig. 1. ⊙, Ackermann's values

indicate that uranium metal is slightly soluble in uranium dioxide, that is, that the stoichiometric range of uranium dioxide extends slightly on the oxygen-deficient side of the ideal formula, at the quenching temperature of the arc furnace (estimated as between 2,500° C. and 1,600° C.). Extrapolating from the recent data of Ackermann[2] for the cell dimensions of oxygen-excess uranium oxides, it can be deduced that the limiting composition of the oxygen-deficient phase is $UO_{1\cdot99}$ to $UO_{1\cdot97}$ (Fig. 1).

(*B*) A minor phase was present to the estimated extent of 2–6 mole per cent. Its diffraction pattern consisted of seventeen lines, the *d* values of which are irreconcilable with the presence of any of the following phases: (*a*) the reported cubic lower oxides—uranium monoxide[3] with $a_0 = 4\cdot92$ Å., Zachariasen's supposed $UO_{1\cdot75}$ (ref. 3) with $a_0 = 5\cdot477$ Å., or the UO_{2-x} of Perio and Hering[4] with $a_0 = 5\cdot484$ Å; or (*b*) the α- or γ-allotropes of uranium metal. α-Uranium, stable between room temperature and 667° C., is orthorhombic with *a* 2·852 *b* 5·865 *c* 5·495 Å. (refs. 2, 5); γ-uranium, stable above 767° C., is body centred cubic, $a_0 = 3\cdot43$ Å. (refs. 2, 3). However, the interplanar spacings agree fairly well with those of lines in the complex diffraction pattern[6] of β-uranium, the form stable only between 667° C. and 767° C. (Table 1).

Table 1. Comparison of X-ray Data for the Minor Phase with the X-ray Data for β-Uranium

β-Uranium (6)		Minor phase		β-Uranium		Minor phase	
d Obs.	*I* Obs.	*d* Obs.	*I* Obs.	*d* Obs.	*I* Obs.	*d* Obs.	*I* Obs.
2·827	10	2·77	w.	1·163	20	1·16	w.
2·696	4			1·116	18		
2·649	6			1·079	5		
2·612	70	2·58	w.	1·073	9		
2·536	53			1·051	24		
2·500	41	2·50	m.	1·037	22		
2·438	48			1·035	19		
2·370	100	2·39	m.	1·022	36	1·02	w.
2·313	58			1·005	15	1·01	w.
2·270	20	2·28	w.	0·9947	18		
2·175	19	2·17	m.	0·9796	25		
2·054	11			0·9742	24		
2·011	9			0·9621	20		
1·975	9	1·96	v.w.	0·9489	23	0·954	w.
1·712	11	1·71	w.				
1·692	14			m, Medium; w., weak; v.w., very weak; v.v.w., very very weak.			
1·631	25						
1·615	10						
1·543	28	1·56	w.				
1·526	45						
1·513	40						
1·502	42						
1·479	37	1·48	w.				
1·467	19						
1·457	17						
1·442	21						
1·415	13						
1·304	24	1·30	w.				
1·289	6						
1·243	29						
1·214	22						
1·207	22	1·21	w.				
1·193	9						
1·184	17						
1·177	10	1·17	v.v.w.				

Proof that the minor phase was uranium metal was afforded by the following experiment. One of the fused samples, of composition $UO_{1\cdot883}$, was powdered and sealed into an X-ray capillary, both operations being carried out inside a sealed, evacuated apparatus. The X-ray pattern then showed that while the major phase was unchanged, the minor phase had altered; its diffraction pattern could be completely indexed in terms of the α-uranium structure (Table 2).

Table 2. Comparison of X-ray Data for the Minor Phase (after Powdering) with the X-ray Data for α-Uranium

α-Uranium (5)		Minor phase		α-Uranium		Minor phase	
d Obs.	*I* Obs.	*d* Obs.	*I* Obs.	*d* Obs.	*I* Obs.	*d* Obs.	*I* Obs.
2·563	s.	2·562	w.	1·012	m.	1·014	v.w.
2·521	s.	2·521	w.	0·992	m.	0·993	v.w.
2·473	s.	2·475	w.	0·945	m.		
2·274	s.	2·275	w.	0·936	m.		
1·778	s.	1·781	w.	0·922	w.m.		
1·532	s.	1·533	v.w.	0·878	w.m.		
1·436	m.	1·437	v.w.	0·843	s.	0·844	v.v.w.
1·387	m.			0·815	s.	0·816	v.v.w.
1·260	m.						
1·238	s.			s, Strong; m., medium; w., weak; v.w., very weak; v.v.w., very very weak.			
1·153	m.	1·153	v.w.				
1·114	m.						
1·088	w.m.						

Thus uranium dioxide decomposes at its melting point, first to an oxygen-deficient oxide and then to metallic uranium (Fig. 1). Under the conditions of our experiments the metal, dispersed through the fused oxide, appeared to be retained in the highly metastable β-modification, but reverted to the stable α-uranium when the sample was ground up in the absence of oxygen.

Further work on the uranium–uranium dioxide system at high temperatures is being carried out and will be described elsewhere.

Two of us (J. O. S. and M. J. B.) wish to thank the Australian Atomic Energy Commission for research grants, during the tenure of which this work was carried out.

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Electron Spin Resonance Absorption of the Biradical Molecular Complex, *p*-Phenylenediamine-chloranil

According to Mulliken's quantum-mechanical theory the lowest state of a molecular complex *A.D*, where *A* and *D* stand for the electron acceptor and donor, respectively, is chiefly a non-bonding state, and the next excited state is a dative state A^-–D^+ (ref. 1). Kainer *et al.*[2–5] have considered the existence of molecular complexes where the ionic state is the lower of these two states and studied the electron spin resonance and the other properties of a number of

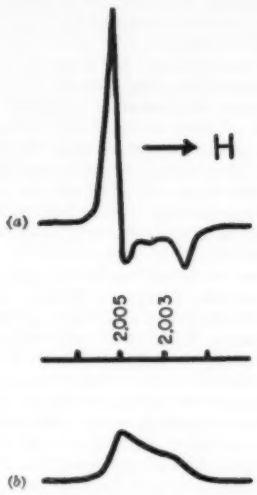

Fig. 1. Electron spin resonance absorption spectrum of the molecular complex *p*-phenylenediamine-chloranil

molecular complexes which consist of aromatic diamines and quinones.

It has been known that even in a biradical molecule of Chichibabin's hydrocarbon type, or its analogues, two unpaired electrons are only weakly coupled[6,7]. Therefore, it seemed that it might be possible to resolve the resonance absorption of aromatic diamine-halogenoquinone complexes because of a fairly large difference of *g*-value between these two components in ionized forms. With this hope we re-examined the electron spin resonance absorption of some aromatic diamine-halogenoquinone complexes using a high-resolution spectrometer[8]. The measurements were at a frequency of 9 kMc./s. and at room temperature.

Only in the case of *p*-phenylenediamine-chloranil was the resonance absorption clearly resolved and the two peaks were definitely correlated with the component ions. It was found that the shape of the resonance absorption curve depends, to some extent, on the preparation. A typical spectrum is shown in Fig. 1. The spectrum consists of a sharp peak with a *g*-value of 2·005 and a slightly broader one with 2·003. The former *g*-value is in good agreement with that of the potassium salt of tetrachloro-*p*-benzosemiquinone, 2·0048, and the latter with those of Wurster's blue salts, 2·0028 for the ferricyanide, and 2·0033 for the picrate[9]. The spectrum of N,N,N′,N′-tetramethyl-*p*-phenylenediamine-chloranil could not be well resolved but was found to be highly asymmetric. The main peak is again located at the position of tetrachloro-*p*-benzosemiquinone, but the slope at low magnetic field side is much steeper.

Our results seem to show that these molecular complexes, which we may call salts, consist of ionized components, and the electronic interaction between positively charged diamine and negatively charged quinone molecules is not strong. Both these molecular complexes are unstable. The colour of the latter sample changed from dark red to blue on standing for a week and its spin concentration decreased by a factor of ten. The same blue product could be obtained by mixing warm benzene solutions of the components. Tetrabromo-*p*-benzosemiquinone has a higher *g*-value than its chloro-analogue; however, the molecular compounds with bromanil gave absorptions which were too broad to be resolved.

We also detected a weak resonance absorption in *p*,*p*-diethoxybinaphthostilbene-chloranil[10]. It is not clear whether or not this molecular complex is of the ionic type like aromatic diamine-quinone.

The spin concentration in these aromatic diamine-quinone complexes has been found to be independent of temperature[3,5]. This property has not yet been well explained[5]. In connexion with this, it may be interesting to recall the observation that polycyclic aromatic hydrocarbon-iodine complexes, where the ground-state is supposed to be non-bonding, show strong electron spin resonance absorption[11]. No change of spin concentration in these molecular complexes was observed in the range from 77° K. to room temperature.

We wish to thank the National Research Council of Canada for grants in aid of this work.

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Spectrum of Delayed Fluorescence in Phenanthrene Vapour: a Criterion of Purity

In addition to the normal fluorescence emission with a decay constant of $\sim 10^9$ sec.$^{-1}$, a slow component with a decay constant of $\sim 10^3$ sec.$^{-1}$ has been detected by Dikun in the luminescence of phenanthrene vapour[1]. On the grounds that the spectra of both components are identical, Williams[2] has attributed this delay to the reversible formation of an excited dimer, from normal and electronically excited molecules, which has a life-time of the order of a millisecond.

In view of the remarkable similarity between the phenanthrene vapour emission spectra obtained by Dikun and the fluorescence spectrum of anthracene vapour, we decided to repeat this work using Eastman Kodak phenanthrene of highest purity, which was treated with maleic anhydride[3] until a saturated solution in hexane was completely transparent above 355 mμ; this places an upper limit of one part in 25,000 on the concentration of anthracene impurity.

The phenanthrene vapour at 9·6 mm. and 260° C. was irradiated in a 'Pyrex' cell by the 313 mμ line isolated from a high-pressure mercury-vapour lamp by an alkaline chromate filter[4]. Emission spectra were photographed on a small Hilger quartz spectrograph, a locally constructed phosphoroscope being used to isolate the slow component; a medium Hilger

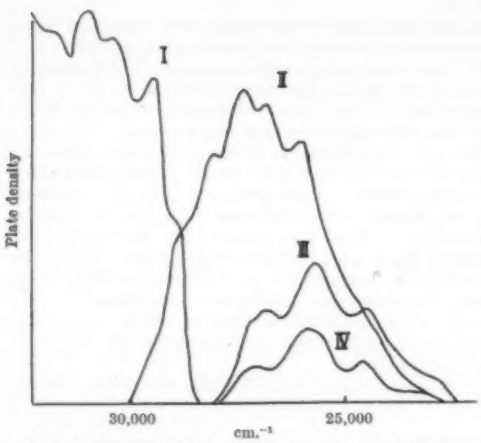

Fig. 1. Absorption (I) and emission (II) spectra of phenanthrene vapour at 9·5 mm. and 260° C. together with spectrum of delayed fluorescence (IV) and of pure anthracene vapour (III). Emission spectra were excited by the mercury 313 mμ line in each case

quartz instrument and hydrogen discharge lamp were used to photograph the absorption spectrum of the vapour at the same pressure and temperature.

Microdensitometer tracings of the plates obtained are shown in Fig. 1, together with the fluorescence spectrum of anthracene vapour excited by the 313 mμ line[5]. The delayed spectrum IV coincides in peak position and relative peak intensity with that obtained by Dikun and with the fluorescence spectrum of anthracene III; clearly it is not identical with the unsectored spectrum II and in so far as the fluorescence spectrum is a molecular characteristic it must be attributed to anthracene present as impurity.

If it is assumed that the anthracene in our phenanthrene sample is completely vapourized, its maximum possible pressure under the conditions described is $3{\cdot}8 \times 10^{-4}$ mm., corresponding to an optical density of $\sim 10^{-5}$ at 313 mμ. Thus collisional sensitization of anthracene by excited phenanthrene molecules is extremely unlikely, as is any mechanism involving the absorption of incident radiation by anthracene. We suggest, therefore, that anthracene is sensitized by collision by the excited phenanthrene dimer, which is simultaneously quenched; the lifetime of this dimer in the absence of anthracene is not known, but cannot be less than a millisecond, and in consequence the half-quenching pressure of anthracene required is at the most some 10^{-4} mm., which is within the estimated limit of impurity concentration. The absence of phenanthrene bands from the spectrum of the slow component IV suggests either that the excited dimer does not dissociate or that the quenching process is extremely efficient; this would be expected on the grounds of spin conservation since the excited dimer is in a singlet state[6].

A further requirement for efficient transfer concerns the coincidence of energy-levels in the donor and acceptor, and in this case affords an estimate of the maximum heat of formation E of the dimer from normal and excited molecules. Since the energy transferred is at least 26,400 cm.$^{-1}$ and the first excited singlet state of phenanthrene lies 28,300 cm.$^{-1}$ above the ground-state[7]:

$$E \leqslant 5{\cdot}4 \text{ kcal.}$$

which may be compared with the value ~ 6 kcal. for the heat of dissociation of the excited anthracene dimer found from the temperature dependence of self-quenching (ref. 8 and Stevens, B., and McCartin, P. J., unpublished work).

The marked resemblance between the unsectored phenanthrene spectrum presented by Dikun and the anthracene vapour fluorescence spectrum is indeed surprising. An optical density of 0·3 at 365 mμ quoted by this author suggests that the anthracene concentration in his sample is sufficient for its fluorescence spectrum to be excited directly, while the absence of phenanthrene bands could be due to complete self-quenching at the higher pressures used in his investigations.

Finally, it may be noted that if the proposed mechanism is correct, the delayed spectrum is virtually the molecular fluorescence spectrum of anthracene. This arises from a fortuitous combination of circumstances whereby a measurable fluorescence intensity of anthracene vapour at a concentration not exceeding 10^{-6} mol./l. is sensitized by an exceptionally long-lived species which is a secondary product of absorption in a region that does not overlap the emission spectrum of the acceptor.

We wish to thank the Safety in Mines Research Establishment for the loan of spectrographs, and one of us (E. H.) acknowledges the award of a maintenance grant from the Department of Scientific and Industrial Research.

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BIOPHYSICS

Sedimentation of Deoxyribonucleic Acid isolated under Low Hydrodynamic Shear

Bacteriophage deoxyribonucleic acid in solution was recently demonstrated to be degraded by moderate hydrodynamic shear gradients[1]. This observation provoked the question whether the 6–8,000,000 molecular weight, usually observed in purified preparations of deoxyribonucleic acid from animal or bacterial sources, is in any way indicative of the size of the molecules of the acid in the living cell, since in none of the common methods used for purifying deoxyribonucleic acid are precautions taken to minimize shearing.

Anderson *et al.*[2] attributed to deoxyribonucleic acid the high, shear-labile viscosity they detected in strong salt solutions of nuclear material. Unfortunately, such solutions contain protein, which could cross-link deoxyribonucleic acid. This communication briefly reports the isolation from trout sperm of shear-sensitive purified deoxyribonucleic acid of high sedimentation coefficient.

Fish sperm were used because the nuclei contain no ribonucleic acid and are easily isolated by plasmolysis

and centrifugation[3]. Mr. B. Hazen of the U.S. Fish and Wildlife Service, Nashua, New Hampshire, generously provided several samples of freshly shed milt.

A number of experiments, which will be described elsewhere, suggested that although disrupting a suspension of fresh sperm nuclei by sodium dodecyl sulphate[4] or strong salt produces an extraordinarily viscous solution, relatively little of the deoxyribonucleic acid is molecularly dispersed; instead, it appears likely that the deoxyribonucleic acid occurs in the form of extremely long, tangled molecules. To obtain deoxyribonucleic acid free of occluded protein it was necessary to degrade these long molecules by applying a small shearing force.

The following preparative technique was used: A dispersion of nuclei (about 0·1 mgm. nitrogen per ml.) in 0·01 *M* sodium chloride was mixed with 1/11 volume of 5 per cent sodium dodecyl sulphate in 45 per cent ethanol[4]. After standing for 1 hr. at room temperature the solution was passed twice through a 60-cm.-long glass capillary tube, applying a calculated mean shear of 800 sec.$^{-1}$. One-third volume of 4 *M* sodium chloride was added, and after gentle shaking for a further hour, the solution was centrifuged 1 hr. at 18,000*g*. Deoxyribonucleic acid (nitrogen/phosphorus ratio 1·70) was precipitated from the water-clear supernate by ethanol. About 25 per cent of the acid in the sperm was recovered. This presumably reflects the efficiency of dispersing the deoxyribonucleic acid; by applying higher shear forces to the solution the yield of acid increased, but the mean sedimentation coefficient of the product fell.

The secondary structure appeared to be intact since the deoxyribonucleic acid showed a 30 per cent hyperchromicity at 260 mμ on alkalination[5]. For physical study the deoxyribonucleic acid was redissolved in 0·01 *M* sodium chloride under gentle agitation.

The ultracentrifuge techniques have been previously described[1]. The cells were filled at a mean shear-rate of 1,000 sec.$^{-1}$. A typical distribution of the sedimentation coefficients in one of these preparations is shown in Fig. 1. The sedimentation diagram was unchanged after treatment with versene, trypsin, or chymotrypsin. Fig. 1*C* shows the corresponding distribution in deoxyribonucleic acid isolated from the same batch of milt by the method of Kay, Simmons, and Dounce[4].

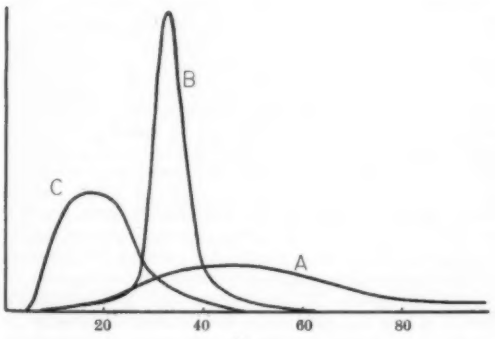

Fig. 1. Distribution of sedimentation coefficients in deoxyribonucleic acid. *A*, Prepared at low shear; *B*, sample *A* degraded by shear; *C*, prepared by method of Kay *et al.* (ref. 4). Solvent: 0·2 *M* sodium chloride, 0·015 *M* sodium citrate

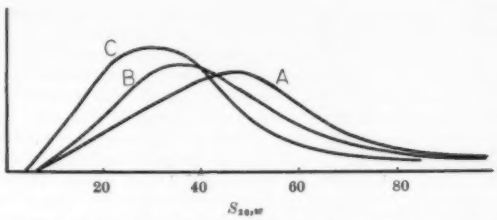

Fig. 2. Distribution of sedimentation coefficients in deoxyribonucleic acid. *A*, Intact; *B*, sheared once; *C*, sheared thrice. Solutions heated before centrifugation. Solvent: 0·2 *M* sodium chloride, 0·015 *M* sodium citrate. Ordinate scale twice that in Fig. 1

Deoxyribonucleic acid prepared in the manner outlined above and sheared at 40,000 sec.$^{-1}$ is shown in Fig. 1*B*. The shearing lowered the viscosity of the solution 25 per cent (as measured in a simple Ubbelohde viscometer at relatively high shear). When the solution was sheared twice more, the peak appeared even sharper, and the maximum dropped about 2 *S* (Svedberg units), while the viscosity dropped a further 10 per cent. Two anomalies are apparent in these results: (1) the viscosity changes are disproportionate to the drastic change in the sedimentation diagram on the first shearing, and the small change afterwards; (2) if the mechanism of the shear degradation is that previously discussed[1] the shearing should either halve the molecule or leave it intact, and it is unlikely that a drop from 32 *S* to 30 *S* represents a halving of the molecular weight.

However, the width of the sheared diagrams increased with dilution, and it appeared probable that the boundary was self-sharpened. This effect was not obviated at extreme dilution, but disappeared when the solutions were heated.

Briefly heating deoxyribonucleic acid solutions of moderate ionic strength to 100° C. destroys the ordered helical configuration of the molecule[6] and broadens the sedimentation distribution diagram[7], usually without decreasing the molecular weight. The broadening of the sedimentation diagram probably reflects an increased polydispersity of shape, together with some molecular degradation and some aggregation through re-formed hydrogen bonds[8]. Since it is unlikely that aggregation and degradation could fortuitously counterbalance if either process occurred to a great extent, it seems probable that at least the major features of the distribution of the sedimentation coefficients are preserved in the heated preparations.

Fig. 2 depicts the sedimentation diagrams of sheared deoxyribonucleic acid samples after heating. The fact that these distributions appear qualitatively consistent with the viscosity studies supports the suggestion that the diagrams approximate the molecular size distribution which was previously concealed in the hypersharp boundaries.

Under the brief shearing a fraction of the susceptible molecules escaped degradation each time. The only unexpected feature of the diagrams was a persistence of the 'tail' on the high *S* side. Since this material was not shear-labile, it might comprise aggregates of low asymmetry, possibly artefacts produced by the heating.

A number of observations indicated that self-sharpening occurs whenever the change of concentration (dc/dr) at a point within the boundary is sufficiently high. Thus, on shearing, the scission of the larger molecules increased dc/dr on the low *S* side

of the boundary, giving rise to an artificial sharpness which over-emphasized the effect of the shearing.

In summary, it has been shown that deoxyribonucleic acid of unusually high sedimentation coefficient can be prepared. If these results can be extended to deoxyribonucleic acid from somatic tissues, it appears to me that at present no limit can be set to the length of the molecule of deoxyribonucleic acid *in vivo*. Protein bridges may exist along these 'molecules', but, until some evidence for them is forthcoming, it is simpler to imagine that the double helix persists uninterruptedly—perhaps for the length of a chromosome[9].

I am indebted to Prof. Francis O. Schmitt and Prof. Cyrus Levinthal for valuable discussions in the course of this work, and to Mrs. K. Y. Ho for technical assistance.

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Lubrication of Mammalian Joints

The experiments and arguments of McCutchen[1] and Lewis and McCutchen[2] appear to confirm the theory of lubrication of mammalian joints first put forward twenty-seven years ago with particular reference to the intra-articular fibrocartilages and later developed in connexion with particular problems of articular structure, general and special[3]. The essence of that theory is that there is a sensibly thick film of synovial fluid between articular surfaces while the joint is in motion, and that this fluid is not only maintained between the surfaces but also flows between them in the direction of motion in accordance with the laws of viscous hydrodynamics. The question of the origin of the fluid was left in abeyance, being a physiological rather than a mechanical problem.

It is an axiom, too often unstated, that the flow of lubricant film while it is acting requires that the fluid shall adhere to the fixed and the moving surfaces; this is tantamount to saying that these surfaces shall be thoroughly soaked with fluid. Movement of one of the surfaces will then necessarily produce a laminar flow if the fluid be viscous, as is easily demonstrated by simple physical models at speeds commensurate with those found in our joints. The structural basis for the sponge-like character of articular cartilage has already been shown by myself[4]. This structure differs markedly from that described by Benninghoff, referred to in the communication from Lewis and McCutchen. The late Prof. Benninghoff told me verbally that he had not examined articular cartilage by the methods given in the preceding reference. Lewis and McCutchen have shown that the articular sponge not only soaks up fluid, thus ensuring its adhesion to the bearing surfaces, but also permits it to be squeezed out, thus ensuring an instantaneous formation of a lubricant film which can then itself be moved as stated above. Such a rapid formation of lubricant fluid is essential in the joints where the range of movement is small by engineering standards and also alternates rapidly in direction. It should be stressed, however, that any theory of articular lubrication must cover all the phenomena of structure within the joint cavity, and should account for the presence, shape and disposition of soft structures (for example, fatty pads) and ancillary deformable structures (for example, articular disks) found in certain joints where the general theory of viscous lubrication indicates a need for their presence. The 'weeping lubrication' spoken of by Lewis and McCutchen appears to complete the existing theory rather than to supplant it, and is a valuable addition to our knowledge of biomechanics.

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While we agree with Prof. MacConaill that there is a thick layer of fluid over most of the area between the articulating surfaces of a joint, we none the less insist that how it gets there is a mechanical rather than a physiological problem. When a joint is loaded, the fluid between the surfaces will be at high pressure, and this must be overcome by whatever process supplies the fluid. Weeping lubrication solves the problem by automatically pressurizing the reservoir from which the fluid is supplied. This is accomplished at the expense of gentle contact at a few high spots in order to press the sponge-like cartilages back into the fluid they are soaked with.

Hydrodynamic lubrication can, in principle, drag fluid into the high-pressure region, but the amount is very small. A simple calculation[1,2] for the knee joint of a sheep shows that, even were the shapes and motion of the joint surfaces ideal, the amount of fluid which can be brought between the articulating surfaces in one swing of the leg at walking speed is equivalent to a layer no greater than half a micron thick. We have shown that the weeping process can provide 30–70 times this amount of fluid; so it seems unlikely that the hydrodynamic contribution is very important. At lower speeds, hydrodynamic lubrication seems even less likely, because the amount of fluid supplied per swing follows the half-power of the sliding speed. If one follows the hydrodynamic theory down to extremely low sliding velocities in the hope of being helped by the unusual properties of synovial fluid[3], one finds that there is no appreciable increase in viscosity of the lubricant until the sheep walks at less than 10^{-7} m.p.h., at which speed the

lubricating film is less than 10 Å. thick. Few surfaces are this smooth, and, in practice, boundary lubrication conditions would set in at far higher speeds.

Failure of the lubricant film at low sliding speeds, which is a standard feature of hydrodynamic lubrication[3], ought to lead to a high coefficient of starting friction. Charnley[4] actually measured starting friction and found that no more force was required to start a joint sliding than to keep it sliding.

The precise structure of the cartilage is not of prime importance. What is important is that it should act as a sponge in which fluid can move easily in a direction normal to the articular surface; that this does occur is confirmed by the experiments detailed in the second half of our original communication. It is also important that the lateral permeability should not be too high, otherwise the cartilage would rapidly collapse when the load was applied. Our experiments gave no indication of a high lateral permeability, but this aspect of our hypothesis does require more detailed, preferably quantitative, study.

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BIOCHEMISTRY

Preparation and Some Properties of a Soluble Ribonucleic Acid in Yeast

The function of soluble ribonucleic acid in the transfer of activated amino-acids to the microsomal ribonucleoprotein particles has been correlated to the presence of a specific terminal *-pCpCpA* group[1-3], and the occurrence of pseudouridylic acid in the molecules[4]. One of the basic requirements for the full understanding of the structural basis of the function of soluble ribonucleic acid would be the preparation of a ribonucleic acid sample which is homogeneous, unaltered, and having a functional activity not different from that present in the living cells. The principal purpose of this study has been to establish the technique whereby a sample of acid which satisfies the above requirements is prepared. The attempt towards this direction led to preparation of an active ribonucleic acid sample which is homogeneous when judged by electrophoretic examination and sedimentation analyses.

It has been reported that in yeast cells the bulk of the active ribonucleic acid is localized in the fraction soluble at *p*H 5·0 or *p*H 5·3 of the 105,000*g* supernatant of the homogenate[4]. A crude sample of the acid obtained by the phenol method of Kirby[5] from the *p*H 5·0 supernatant fraction was contaminated with polysaccharide which has, however, little effect on the incorporation of leucine labelled with carbon-14 into the ribonucleic acid under the conditions previously described[4]. The sample of crude acid was dissolved in 0·001 *M* potassium phosphate buffer at *p*H 7·1, and shaken with 'Ecteola'-cellulose[6] for 5 min. in the cold. About 90 per cent of ultra-violet-absorbing substance originally present in the crude ribonucleic acid preparation was adsorbed on 'Ecteola', whereas all polysaccharides remained uncombined. The 'Ecteola'–ribonucleic acid complex was thoroughly washed with the buffer to remove the unadsorbed materials. The bulk of the ultra-violet-absorbing substance could then be released with 0·3 *M* sodium perchlorate at *p*H 7·1, and recovered by ethanol precipitation. Under these conditions, the ribonucleic acid prepared from the cytoplasmic ribonucleoprotein particles was held firmly to 'Ecteola' and did not come out with 0·3 *M* sodium perchlorate. About 75 per cent of ultra-violet-absorbing substance in the original crude sample of ribonucleic acid was recovered by precipitation by ethanol. Electrophoretic examination revealed the removal of polysaccharides. However, a small peak was detectable slightly ahead of the main acid peak. This fast component was removed completely by 24-hr. dialysis. An electrophoretically homogeneous sample of a soluble ribonucleic acid could thus be obtained. A rapid 'Ecteola' treatment seems to be essential for the successful preparation. An extensive degradation and inactivation of the ribonucleic acid were observed, when the column chromatographic fractionation on 'Ecteola' of the ribonucleic acid was tried.

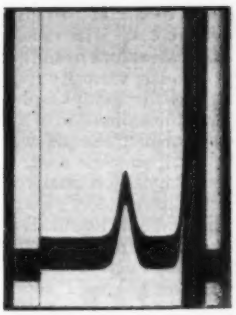

Fig. 1. Sedimentation pattern of purified yeast soluble ribonucleic acid. Picture taken after 24 min. at 56,900 rev./min. in a synthetic boundary cell. 1·6 per cent solution in 0·1 *M* sodium chloride–0·03 *M tris*(hydroxymethyl)aminomethane at *p*H 7·1

The purified sample was also homogeneous in the sedimentation analyses (Fig. 1), giving a sedimentation constant of $S^{0}_{20} = 4{\cdot}0$, extrapolated from the values obtained at three sample concentrations in 0·1 *M*

Table 1. Some Properties of Soluble Ribonucleic Acid compared with those of Ribonucleic Acid prepared from Cytoplasmic Ribonucleoprotein Particles of Yeast Cells (*Saccharomyces cerevisiae*)

	λ max.	ϵ(P)	λmin.	ϵ(P)	$100\,[\eta]_{20}$ ml./gm.	S^{0}_{20}	Mol. wt.	Axial length a(Å.)	Axial length b(Å.)
Soluble ribonucleic acid	258	6,980	230	3,330	0·05	4·0	27,000	133	19
Ribonucleic acid from cytoplasmic ribonucleoproteins	258	7,620	231	3,100	0·54	22 (main)* 19 4 ~ 5	1,100,000	—	—

All measurements were done in 0·1 *M* sodium chloride–0·03 *M tris*(hydroxymethyl)aminomethane at *p*H 7·1. Molecular size and shape for soluble ribonucleic acid were calculated assuming partial specific volume = 0·58, and the molecular model of a rigid ellipsoidal rod.
* Three peaks were detected. No correction for dependence on temperature and concentration.

sodium chloride — 0·03 *M* *tris*(hydroxymethyl)-aminomethane at *p*H 7·1. The molecular weight of the ribonucleic acid calculated from the sedimentation constant and the intrinsic viscosity ($[\eta]_{25} = 0{\cdot}05$) was 27,000 (Table 1). The nitrogen/phosphorus ratio of the product was 1·63. Contamination of deoxyribonucleic acid in the most purified sample was around 0·25 per cent relative to ribonucleic acid.

The nucleotide composition analyses by 'Dowex-1' column chromatography[7] confirmed the previous findings of the predominant localization in the soluble ribonucleic acid of pseudouridylic acid[4,8] and other minor nucleotide components[8].

The purified ribonucleic acid combined L-leucine in the proportion of 2·86 mμ*M*/mgm. ribonucleic acid under the conditions described previously[4]. The value was about 40 per cent higher than that obtained when the crude sample of ribonucleic acid was tested. This seems to be not due to the inhibitory action of contaminated materials in the crude acid, but rather to the removal of inactive ultra-violet-absorbing substances during the purification.

Although the ribonucleic acid obtained is fairly homogeneous from the criteria here adopted, it is not known at the present time whether the acid is a mixture of ribonucleic acids each of which is specific for the attachment of individual amino-acids[9].

A full account of this work will be published later.

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Biosynthesis of Chlorophylls a and b in *Chlorella vulgaris*

We have shown that both carbon atoms of glycine were incorporated into chlorophyll *a* when *Chlorella vulgaris* was incubated with ^{14}C-glycine for a period of 1 hr. During this period no carbon-14 from the carboxyl group could be detected in chlorophyll *b*, whereas the incorporation of the carbon from the methylene group was several times higher than in the case of chlorophyll *a*. Only after longer periods of incubation with 1-^{14}C-glycine was the isotope found in chlorophyll *b* as well.

The purity of the glycine samples (1-^{14}C-glycine and 2-^{14}C-glycine, specific activities about 50 μc. per mgm.) was determined chromatographically; the radioautograms contained no impurities. *Chlorella vulgaris*, strain '211/11*m*' or 'Cornell 11' (received from the Culture Collection of Algae and Protozoa, University of Cambridge), was grown in sterile liquid cultures in volumes of 100 ml. per flask. The composition and the preparation of the medium were described by Della Rosa *et al.*[1]. In order to obtain a homogeneous algal culture of the 'D_A type'[2], the Tamiya procedure of 'synchronous culture' has been adopted (16 hr. light of 1 k.lux and 8 hr. of darkness). After maximal verdancy of the cells was achieved, 10 μc. ^{14}C-glycine were introduced. Samples were then withdrawn after various periods of incubation under 1 k.lux of light. The yield per flask amounted to about 100–150 mgm. of dry algae. 'Raw chlorophyll', free of xanthophylls, was extracted from the frozen material according to Strain and Manning[3] and chromatographed on Whatman No. 1 paper impregnated with saccharose (Sporer *et al.*[4]) using Bauer's solvent[5]. Chlorophylls *a* (R_F about 0·65) and *b* (R_F about 0·35) were eluted with ethyl ether and determined spectrophotometrically, employing the absorption coefficients given by Smith and Benitez[6]. The wet combustion of the chlorophyll samples was carried out as described by Van Slyke and Folch[7], using inactive glucose as carrier, and the carbon dioxide converted into barium carbonate. The labelled carbon dioxide set free from the barium carbonate was measured in the gas Geiger counter of Broda *et al.*[8] and calculated to 100 per cent counting yield. The results are presented in Table 1.

Table 1. Incorporation of Carbon-14 from Glycine into Chlorophylls *a* and *b*

Substrate	Time of incubation (hr.)	Specific activity of chlorophyll (c.p.m. × 10^{-4} per mgm. C)					
		a			*b*		
		No.	Results	Average	No.	Results	Average
1-^{14}C-glycine	1	I	1·29	1·02	I	0	0
		II	0·91		II	0	
		III	0·85		III	0	
	6	I	4·96	5·25	I	5·36	6·16
		II	5·17		II	6·71	
		III	5·62		III	6·43	
2-^{14}C-glycine	1	I	0·59	0·68	I	3·09	2·41
		II	0·75		II	—	
		III	0·70		III	1·73	
	6	I	8·80	9·38	I	21·8	15·8
		II	6·55		II	9·72	
		III	12·8		III	—	

Della Rosa *et al.*[1] found in experiments in which the period of incubation lasted several days that, in contrast to the biosynthesis of hæm, not only the methylene carbon but also the carboxyl carbon of glycine is utilized in the synthesis of chlorophylls *a* and *b*. In view of the fact that the isotope concentrations in both chlorophylls were of the same order of magnitude they decided against the current theory that chlorophyll *b* may be derived from chlorophyll *a*. Since our results after 6 hr. of incubation are similar to those of Della Rosa *et al.*, and since after 1 hr. of incubation (that is to say, in the beginning stages of biosynthesis) the uptake of carbon-14 from the two sources is different for the two chlorophylls, the suggestion that the path of biosynthesis of chlorophylls *a* and *b* may be different seems quite reasonable.

It would appear from our work that in the biosynthesis of chlorophyll *b*, as in the synthesis of hæm, the methylene carbon of glycine plays the main part, and that this process may be simpler or quicker than the incorporation of this carbon into chlorophyll *a*. On the other hand, both carbon atoms are utilized equally well by chlorophyll *a*. The scheme proposed by Della Rosa *et al.*, namely, that the carboxyl carbon is incorporated into the chlorophylls via the citric acid cycle, cannot be accepted, as in this case the carbon-14 concentration in chlorophylls *a* and *b* after 1 hr. of incubation should be of

similar magnitude. As can be seen from Table 1, there is considerable incorporation of the carboxyl carbon into chlorophyll *a* and no incorporation at all into chlorophyll *b* after 1 hr. of incubation.

After 6 hr. the specific activities of both chlorophylls are of the same order, and are always higher on incubation with 2-^{14}C-glycine than with 1-^{14}C-glycine. This observation may suggest some incorporation of the carboxyl carbon of glycine, which takes no direct part in the biosynthesis of chlorophyll *b*, into some other group which may then be equally well used in the synthesis of both chlorophylls.

We are indebted to Prof. E. Broda in Vienna, where our work was started, and to Prof. I. Reifer in Warsaw, where our work was concluded, for helpful discussions.

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Stereospecificity of Enzymic Reactions involving Mevalonic Acid

Most of the biosynthetic studies with mevalonic acid have so far been carried out with the racemic substance labelled with carbon-14. There have been no reports indicating a utilization greater than 50 per cent of DL-mevalonate either *in vivo* or *in vitro* in any enzymic reaction. Thus, Tavormina, Gibbs and Huff[1], who made the discovery that mevalonate was an outstanding precursor of cholesterol, noted that about 43 per cent of the DL-[2-^{14}C] mevalonate was converted in liver homogenates into cholesterol; an observation confirmed by Popják *et al.*[2]. Gould and Popják[3] found that of the dose of carbon-14 contained in DL-[2-^{14}C] mevalonate and injected into mice about 40 per cent appeared in body sterol, 10 per cent in expired carbon dioxide and 50 per cent in the urine. Both Tchen[4] and Levy and Popjak[5,6] observed that in the mevalonic kinase reaction, in the phosphorylation of mevalonate with adenosine triphosphate to 5-phosphomevalonate, no more than 50 per cent of the DL-mevalonate was used by the enzyme. All these observations led to the conclusion that only one enantiomorph of mevalonate could act as substrate in biosynthetic reactions, and this was assumed to be the natural (+) isomer, $[\alpha]_D^{24}$, + 10° (Wolf *et al.*[7]).

We have obtained direct evidence on this question and found that the mevalonate excreted in the urine of animals given DL-mevalonate is of the unnatural optical configuration, and that the 5-phosphomevalonate, prepared enzymically with liver mevalonic kinase[5,6] was an optically active substance.

Three rats, kept in metabolism cages, were given daily in their food 50–100 μmoles of potassium DL-mevalonate mixed with a small amount of DL-[2-^{14}C] mevalonate. The total dose given to the three animals was 201 mgm. (calculated as mevalonic acid lactone). The urine, which was collected and pooled, was brought to *p*H 9 and extracted with chloroform for 20 hr. to remove neutral material; then it was made acid to congo red and extracted again for 20 hr. with chloroform. Nearly all the carbon-14 contained in the urine was recovered in this extract. The second chloroform extract was evaporated under vacuum and the residue distributed between water and ether. The aqueous layer was evaporated to dryness under reduced pressure at 30–40° and the residue distilled at 0·001 mm. of mercury pressure, the bath temperature being raised to 130°. The distillate (105 mgm.) was refluxed with diphenylmethylamine in benzene for 1½ hr. and mevalonic acid diphenylamide (149 mgm.) isolated as described previously[8]. On recrystallization from benzene, 105 mgm. of the amide (m.p. 95–96°) were obtained with $[\alpha]_{589}^{24}$ + 2·2° in ethanol. The results of optical rotatory dispersion measurements, made at a concentration of 1·2 gm./100 ml. in ethanol, are shown in Fig. 1.

Wolf *et al.*[7] gave $[\alpha]_D^{24}$ − 2·0° (in ethanol) for the diphenylamide of mevalonic acid lactone isolated from distillers' solubles. It is apparent from the results that the rats have utilized the natural and excreted the unnatural isomer of mevalonic acid.

5-Phosphomevalonate was prepared, as the barium salt, from DL-mevalonate with liver mevalonic kinase according to the procedure of Levy and Popják[6]. Optical rotatory dispersion measurements were made on an aqueous solution (0·25 gm./100 ml.) of 5-phosphomevalonic acid (after removal of barium); these results are shown in Fig. 2. The specific rotation at 589 mμ was $[\alpha]_{589}^{24}$ − 6·1° and the molecular rotation $[M]_{589}^{24}$ − 13·9°. These observations leave no doubt that the former assumptions as to the specificity of

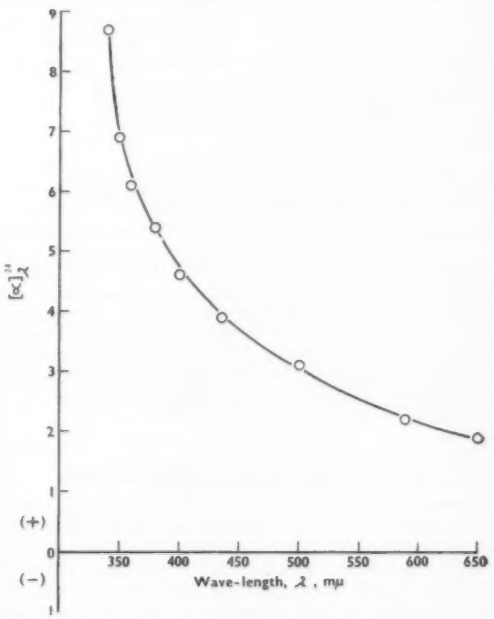

Fig. 1. Optical rotatory dispersion data on the diphenylmethylamide of mevalonic acid in ethanol. The ordinates give specific rotations $[\alpha]_\lambda^{24}$

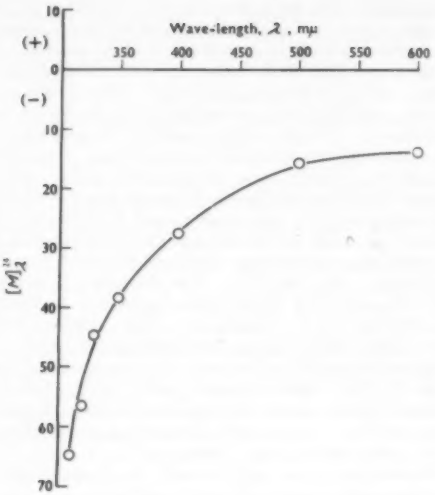

Fig. 2. Optical rotatory dispersion results on 5-phosphomevalonic acid in water. The ordinates give the molecular rotations $[M]^{25}_{\lambda} = [\alpha]^{25}_{\lambda} \times$ mol. wt./100

enzymic reactions for one optical isomer of mevalonic acid are correct.

We are indebted to Dr. C. Sweeley of the National Heart Institute, National Institutes of Health, Bethesda, Md., and to Dr. W. Klyne of the Postgraduate Medical School of London, for the optical rotatory dispersion measurements on the diphenylamide and on the 5-phosphomevalonic acid respectively.

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Glucose-isomerase in Barley Malt

Work in this Institute on the enzymatic breakdown of starch has included above all the qualitative and quantitative determination of products resulting from this breakdown[1]. We have observed that in every case fructose occurred beside the glucose derivatives already in the barley malt extract[2]. The presence of glucose may be attributed to the activity of the amylo-glucosidase enzyme of the barley malt. Among the glucose derivatives maltose is produced by the activity of the well-known β-amylase. The oligosaccharides, from which we succeeded in identifying altogether eight members in two homologous series, beginning with maltotriose and finishing with malto-octaose, were produced by the activity of the amylase. Besides the amylolytic enzymes, there must also be a glucose-isomerase enzyme in action, and it must be its effect which results in the appearance of fructose.

We have verified the presence of fructose by paper chromatography. Fructose is well characterized by the lemon-coloured spot formed in *p*-amino-phenol[3] used as detecting agent. This spot appears only when fructose is present. Among the other carbohydrate products yielded by the breakdown of starch, maltose gives in *p*-amino-phenol an ochre-yellow spot while the oligosaccharides produce spots in colours ranging from reddish yellow to reddish brown. Very characteristic are further for fructose the R_F and R_G values respectively, which could be exactly determined by the control test. In this way the presence of fructose was undoubtedly proved. The quantity of fructose introduced by the malt-extract, and the fructose and saccharose content of the raw material were exactly determined, and it could be observed that at the end of the saccharification process the reaction-mixture contained an amount of fructose which was two or three times higher than that of the raw material. This could be observed no matter whether pure starch of some starch-containing raw material (potatoes or corn) had been chosen for the saccharification. This cannot occur except in the case when, during the breakdown of the starch, enzyme action transforms glucose into fructose. The presence of such an enzyme was proved experimentally; thus we treated a 5 per cent glucose solution with barley malt extract and found that during the reaction the amount of glucose decreased while that of the fructose increased.

We treated a 13–17 days-old malt germinated on a threshing floor with a 5 per cent solution of analytical glucose at 55° C. and 5·2 *p*H, during 2 hr. The carbohydrates were quantitatively determined in both solutions before mixing and in the reaction products after the treatment, using paper chromatography.

The results obtained by quantitative analysis of the chromatogram spots are given in Table 1, every result being for 150 ml. of the solutions.

Table 1

Colour of the spot	$R_F \times 100$	Identified quality of the spot	1*	2† (gm.)	3‡
Lemon-yellow	26·8	Fructose	—	0·76	0·23
Dark brown	24·0	Glucose	4·6	3·92	0·26
Light brown	18·6	Saccharose	—	0·06	0·06
Ochre-brown	15·2	Maltose	—	0·78	0·68
Reddish-brown	11·7	Maltotriose	0·2	0·49	0·36
Yellowish-brown	—	Oligo-saccharides	—	0·52	0·58
Brown	—	Dextrins	—	0·92	0·81
		Totals	4·8	7·45	2·98

* Mixture of 100 ml. 5 per cent glucose solution and 50 ml. distilled water.

† 100 ml. 5 per cent glucose solution and 50 ml. barley malt extract.

‡ Mixture of barley malt extract and 100 ml. distilled water has been chromatographed and analysed.

These results show that, due to the barley malt extract, a quantity of about 1 gm. disappeared from the glucose in solution while the amount of the fructose increased by about 0·5 gm.

Thanks are due to Mrs. Agnes Osztróvszky and Miss Eva Gábor for their kind assistance.

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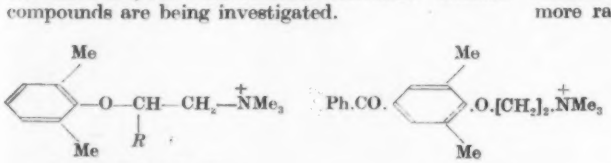
ANIMAL PHYSIOLOGY

Powerful Adrenergic Neurone-blocking Agents related to Choline 2,6-Xylyl Ether Bromide

THE discovery that the functioning of the post-ganglionic sympathetic adrenergic nerves could be impaired by choline 2,6-xylyl ether bromide (I), *TM* 10 (refs. 1, 2), led to a search for compounds having a similar effect, but lacking the parasympathomimetic actions which preclude its use in man[3]. Such a selective blocking action was found in a series of benzyl quaternary ammonium salts[4], and one of these, bretylium tosylate, was eventually shown to be a valuable antihypertensive agent in man[5]. This compound can depress conduction in various nerves, and the specificity of its blocking effect on the sympathetic nervous system seems to be related to its selective accumulation in adrenergic neurones (unpublished work).

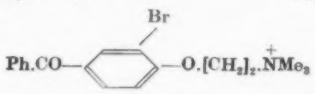
Investigation of analogues of choline 2,6-xylyl ether bromide showed that the β-methyl substituted compound (II) had a similar but more specific action on the adrenergic nerve mechanism[6]. We also have prepared many compounds related to *TM* 10 and screened them for adrenergic neurone-blocking action in the cat, by their ability to relax the nictitating membrane without causing mydriasis. We have found that additional substitution of *TM* 10 in the 4-position by ethoxycarbonyl, acetyl or benzoyl, leads to reduction or abolition of the gross parasympathomimetic effects, with retention or enhancement of the antiadrenergic properties.

One of the most active of these compounds, 172*C*58, is 10–20 times more active than *TM* 10 and is virtually devoid of parasympathomimetic properties. The corresponding bromo-analogue, 225*C*59, has similar adrenergic neurone-blocking properties, but produces muscarine-like effects at high dose-levels. Many chemical variations on the compound 172*C*58, which included branching or lengthening the chain, additional substitution or hydrogenation of the 4-benzoyl group and several variations of the groups in the 2- and 6-positions and in the cationic head, have led to lower activities. Related compounds are being investigated.



I, R=H, II, R=Me

172*C*58*



225*C*59*

* Patents pending

We examined 172*C*58, as its bromide, by the same methods as were used with bretylium[7]. In cats, intravenous doses of 0·05–0·5 mgm./kgm. rapidly depressed for several hours the responses to stimulation of various adrenergic nerves; for example, the increase in heart-rate caused by stimulation of the inferior cardiac nerve, the relaxation of the uterus caused by stimulation of the hypogastric nerve and the contraction of the nictitating membrane during stimulation of the postganglionic cervical sympathetic trunk. These doses lowered the blood pressure of cats in the supine position and caused marked postural hypotension. These effects occurred without depression of the responses to injected noradrenaline or adrenaline; indeed their actions were enhanced, as occurs after sympathectomy. Sweating caused by sympathetic nerve stimulation in the cat was not abolished. Since the postganglionic fibres to the sweat glands are cholinergic, this suggests that the action of the compound is largely confined to adrenergic neurones. The compound showed weak and transient ganglion-blocking properties. No blocking action on the mechanism for release of pressor amines from the adrenals was detected in acute experiments. Neuromuscular paralysis of voluntary muscle occurred with doses about 50 times greater than those which affected the adrenergic nerve mechanism.

The distribution in the tissues of the drug labelled with carbon-14 on one of the quaternary methyl groups showed that it had a high affinity for the adrenergic neurones. 2 hr. after the injection of 1 mgm./kgm. subcutaneously in the cat, the radioactivity in sympathetic ganglia and adrenergic nerve trunks indicated the presence of concentrations of approximately 0·005 and 0·002 μmole/gm., respectively—some five times the highest found in other ganglia and nerves. Furthermore, when the drug was applied topically to adrenergic nerves between stimulating electrodes and a suitable end-organ, the response of the latter was abolished. This was shown in tests using the hypogastric nerve, and the sympathetic fibres of the greater auricular and mesenteric nerves in the rabbit, and also on the postganglionic cervical sympathetic and inferior cardiac nerves of the cat. Like bretylium, the drug has a long-lasting local anæsthetic action. We tentatively conclude that it may impair conduction in those neurones to which it gains access, and that its selectivity of action on adrenergic neurones may be related to its accumulation in these neurones.

The effects of 172*C*58 resemble those of bretylium but are more powerful. However, there are important qualitative differences. The adrenergic neurone-blocking action of 172*C*58 is considerably more rapid in onset and ends sooner, whether the drug is given by intravenous or subcutaneous injection. A related feature is its more rapid effect on isolated nerve-muscle preparations, from which, unlike bretylium, it may be readily removed by washing. Another major difference is that 172*C*58 caused no sympathomimetic effects in cats, except when several times the adrenergic neurone-blocking dose was given.

In two subjects given the drug intravenously and in two hypertensive patients given oral doses, 172*C*58 seemed a less active hypotensive agent than bretylium (Laurence, D. R., Moulton, R., and Rosen-

heim, M. L., personal communication). Its main value would seem to be as a pharmacological tool, its advantages over bretylium being its more rapid and more readily reversible action and its freedom from sympathomimetic properties.

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Significance of Adipose Tissue Lipoprotein Lipase

The post-heparin clearing factor in plasma has the same properties as tissue lipoprotein lipase; this is explained by Korn[1] by the fact that by the action of heparin lipoprotein lipase is released from the tissues in the blood stream. The greatest amount of lipoprotein lipase was found in adipose tissue[2]. A number of observations suggest indirectly the possible physiological significance of this enzyme in adipose tissue, particularly during the mobilization of fat from depots[3–7]. We have tried to elucidate the significance of adipose tissue lipoprotein lipase in rats by investigating the changes of its activity (*a*) after the administration of heparin and (*b*) during the mobilization and deposition of fat.

Immediately after killing the animal we removed the fat of the epididymis, froze it by means of liquid air, ground it to a fine powder from which we removed the fat in the cold, using acetone and ether, and afterwards dried it. The homogeneous powder was extracted with a solution of ammonia, pH 8·5, and the activity of lipoprotein lipase was estimated by determining the non-esterified fatty acids, using Dole's method[9], liberated during incubation with an activated artificial oil emulsion 'Ediol'[8] as a substrate (0·5 ml. extract: 2·5 ml. emulsion, temperature 37° C., incubation period 30 min.) and was expressed per 100 mgm. of dried tissue powder. 1 *M* sodium chloride, which is a specific inhibitor of lipoprotein lipase, inhibited esterolysis; this we consider evidence that in our experiments we actually estimate the enzyme.

The administration of heparin 'Novo' (500 μ/kgm. body-weight intraperitoneally), which causes a marked lipolytic activity of the blood, leads to a marked decrease ($P = 0{\cdot}05$–$0{\cdot}02$) of the lipoprotein lipase activity (Table 1, lines 1, 2). In a further series of experiments we determined the activity of lipoprotein lipase in adipose tissue of rats which had been fasted for 24 hr., and in similarly fasted rats with alloxan diabetes 2, 4 and 6 weeks after the administration of alloxan. No insulin was administered 48 hr. before the experiment. Under these conditions a marked mobilization of fat occurs. For comparison the activity in normal non-fasted animals and in animals which after 48 hr. fasting were re-fed for 20 hr. (Larsen mixture, glucose solution) was determined. In this case fat is not mobilized and in re-fed animals its deposition is much enhanced[10]. Table 1, lines 3 and 4, record the difference in the activity in rats fasting for 48 hr. and in re-fed rats. Fig. 1 summarizes the results of the entire series of experiments in relative figures. It is evident that under conditions when fat is mobilized the activity of lipoprotein lipase in adipose tissue is markedly reduced as compared with the activity in fed animals. Under the condition of an accentuated formation of depot fat in re-fed animals the activity is on the contrary markedly higher as compared with fed animals.

Table 1. Release of Non-esterified Fatty Acids from the Substrate

	No. of rats	No. of samples†	Microequivalent of non-esterified fatty acid ± S.E.	Statistical significance
1* Saline i.p.	15	5	29·02 ± 2·69	$P < 0{\cdot}05$
2* Heparin i.p. 500 μ/kgm.	15	5	21·88 ± 0·94	$P > 0{\cdot}02$
3 48 hr. fasting	18	6	6·32 ± 0·70	$P < 0{\cdot}001$
4 Refeeding	15	5	23·4 ± 3·19	

* Rats in experiments 1 and 2 had free access to food before being killed.
† Every sample was obtained by pooling adipose tissue from three animals.

We assume that in agreement with Korn's concept, which has been confirmed also by other authors[11,14], we can take the decrease of activity in the extract after the administration of heparin as a consequence of the liberation of lipoprotein lipase from adipose tissue. The high enzyme activity during fat deposition, contrary to the low activity during fat mobilization, is striking. The few papers published hitherto on the lipolytic activity of adipose tissue[12,13] do not reveal this fact. This can be explained by the use of a method which is not specific for the estimation of lipoprotein lipase[13]. Only Hollenberg's communication[14], which was published at a time when our work had been already completed and prepared for the press, has arrived at similar results though by a different approach.

As a result of our findings we may conclude, though it is only speculation so far, that during the formation

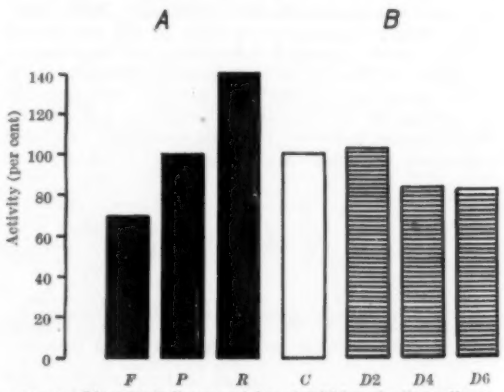

Fig. 1. Lipoprotein lipase activity of epididymal adipose tissue. (*A*). *F*, decreased activity during fasting; *P*, 100 per cent activity in the post-absorptive state; *R*, increased activity after re-feeding. (*B*). *C*, 100 per cent activity of 24-h. fasted control rats; *D2*, *D4*, *D6*, diabetic rats, 2, 4 and 6 weeks, respectively, after administration of alloxan. Rats fasted 24 hr.

of fat in adipose tissue lipoprotein lipase is either synthesized or its activity is enhanced, which would suggest that this enzyme participates in the formation of fat depots. The finding of a reduced activity during fat mobilization must not be taken as evidence that lipoprotein lipase does not participate in this process. It is possible that during this process this enzyme is liberated by adipose tissue, just as after the administration of heparin—but much more slowly—to be transported to another site in the organism where its action is necessary.

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Metabolism of Bemegride labelled with Carbon-14

BEMEGRIDE (β-ethyl β-methyl glutarimide), labelled with carbon-14 in both the α positions, is excreted largely in the urine and to a lesser extent in the bile and faeces when administered to mice, rats and guinea pigs[1]. Chromatograms of urine and bile from these animals were developed by the ascending technique using *n*-butanol/acetic acid/water (12 : 3 : 5, v/v). Autoradiographs of chromatograms of guinea pig bile showed only one spot (R_F 0·88) which was identical in mobility to the control-labelled bemegride. The urine of rats, collected 15–120 min. after administration of labelled bemegride, revealed two spots of R_F values 0·88–0·89 and 0·77–0·81. The faster moving fraction moved as one spot when labelled bemegride was added to the urine before chromatography. The spot with the lower mobility increased in intensity over the 15–120 min. period of urine collection. Urine from mice, 15–120 min. after bemegride injection, showed two spots with R_F values similar to those of rat urine, while urine collected 8 hr. after injection revealed a third spot of R_F 0·40–0·46. This spot became progressively more intense and the faster moving fractions correspondingly less up to 24 hr.

Bemegride labelled with carbon-14 was incubated with rat liver slices in Krebs–Ringer-phosphate solution for 5 hr. at 37° C. and two radioactive spots were revealed on chromatography of the liquid medium. The R_F values, 0·88 and 0·80, corresponded to those obtained from rat urine, suggesting that the liver is the site of bemegride metabolism *in vivo*.

Partition of rat urine with ether followed by chromatography of the two layers showed that the compound of R_F 0·80 was more soluble than bemegride in the aqueous phase (the concentrations were estimated as the relative density of the spots on the autoradiographs). This partition was not changed when determined at *p*H 1 or 7, which indicates that the metabolic fraction is of a similar nature to the unchanged glutarimide. The partition between mouse urine and chloroform revealed that while the spots of R_F 0·88 and 0·79 were distributed between the two layers in a manner similar to that between rat urine and ether, the fraction of R_F 0·45 was confined to the aqueous layer. This shows that the slowest moving fraction is extremely soluble in water.

Failure to detect carbon dioxide labelled with carbon-14 in the expired air of mice receiving labelled bemegride suggests that there is no drastic degradation of the glutarimide molecule. The metabolic products of bemegride detected in the urine of the mouse and rat do not appear to be hydrolysis products of this glutarimide, for the R_F values of β-ethyl β-methyl-glutaramic acid and -glutaric acid are 0·97 and 0·99 respectively in *n*-butanol/acetic acid/water. Succinimide has been shown to be hydrolysed to succinic acid *in vivo*[2] but this metabolic pathway does not appear to be available for the glutarimides. This is supported by the finding that the imide ring of α-ethyl α-phenyl glutarimide remains intact *in vivo*[3]. It is also interesting to note that *Lactobacillus* species are unable to hydrolyse α-amino-glutarimide[4]. β-(2-hydroxyethyl) β-methyl glutarimide, isolated from the urine of a patient who received a large dose of bemegride[5], was found to have an R_F value (0·80–0·83) similar to that of the slower-moving fraction in rat urine, but results from studies in rats involving unlabelled bemegride suggest that these two fractions are not identical.

In the chromatographic location of the hydroxy derivative of bemegride use was made of the technique of Rydon and Smith[6]. This method has proved a simple and valuable means of locating glutarimides on paper chromatograms. The limit of sensitivity for detection is 20–30 μgm. of glutarimide/cm.[2]. By using a 2 per cent starch 1 per cent potassium iodide solution a good definition of the spots is obtained.

It is clear that bemegride, while excreted partly unchanged, is metabolized *in vivo* to produce more water-soluble compounds which probably possess an intact glutarimide ring. The metabolic pathways in the rat and mouse are similar.

Work is in progress to isolate and identify these metabolic products from the urine of mice and rats receiving unlabelled bemegride.

I wish to thank Dr. L. F. Wiggins of Aspro-Nicholas, Ltd., Slough, for supplying bemegride and other glutarimide compounds and also Dr. N. E. W. McCallum for the sample of β-(2-hydroxyethyl) β-methyl glutarimide. I acknowledge receipt of a Nicholas Research Grant of the Welsh National School of Medicine.

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Histochemical Evidence of Aminopeptidase Activity in Rat Pineal Gland

Although various functions have been suggested for the pineal gland[1], very few positive findings have been made concerning this gland[2,3]. In this communication histochemical evidence is given of a strong enzyme activity in the rat's pineal gland capable of splitting L-leucyl-β-naphthylamide hydrochloride. Recent studies[4,5] indicate that this activity is actually due to a group of peptidases, including 'leucine aminopeptidase'.

The pineal glands of about 20 albino rats were studied. After removal from the animals the glands were embedded in brain and rapidly frozen. Fresh frozen cold microtome sections were cut at 30μ. The sections were fixed on coverslips and incubated according to the method of Nachlas *et al.*[6], using diazotized *ortho*-dianisidine or diazonium salt of 4-amino-3 : 2′-dimethyl azobenzene as the coupling agents.

The pineal body of the rat exhibited a strong aminopeptidase activity (Fig. 1). The contrast between the staining of the brain tissue and the pineal tissue was very pronounced ; when the sections were incubated for 30 min. the brain tissue showed practically no staining at all, whereas the pineal tissue was intensely stained. The enzyme activity of the pineal body was not, however, quite as strong as it was in the rat kidney. The aminopeptidase activity seemed to be evenly distributed throughout the gland ; the choroid plexus was infrequently cut together with the pineal body, and it was found to exhibit a moderate enzyme activity.

Pineal bodies of rats of different age groups ranging from 1 to 16 months showed an equal aminopeptidase activity. No sex differences either could be noticed.

Peptidase activity was also tested using *ortho*-acetyl-5-bromoindoxyl as a substrate at an acid medium and diethyl-*p*-nitrophenylphosphate (*E*600) as an esterase inhibitor[7]. This reaction was positive in the rat's pineal body as well, demonstrating cathepsin-*C*-like peptidase activity.

Fig. 1. Leucine aminopeptidase activity in pineal body of a normal adult rat. The choroid plexus beneath the gland shows enzyme activity as well, but the background staining of the brain tissue is due to decomposed diazonium salt (incubation time, 30 min.). (× *c.* 40)

So far as the proposed hormone production of the pineal gland is concerned, the present finding may be of interest. Pearse and Tremblay[8] have recently found an interesting correlation between the hormone production of the rat parathyroid gland and its content of histochemically demonstrable leucine aminopeptidase. The parathyroid hormone, on the other hand, is known to be a mixture of polypeptides. The existence of aminopeptidase activity can be taken to suggest secretion of some agent of a protein nature by the rat pineal gland.

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Clearances of Endogenous α-Ketoglutaric and Pyruvic Acid in Man

The clearances of endogenous α-ketoglutaric and pyruvic acids were investigated in six healthy persons and in ten patients with damaged kidney parenchyma. All persons were confined to bed during the whole experiment. α-Keto-acids were determined after their conversion to corresponding hydrazones which were separated by paper electrophoresis[1].

In all patients with kidney damage the creatinine clearance was lowered. The urine was collected in eight 2-hr. portions during a day and in two 4-hr. portions in the course of a night. (The mean values of clearances of α-ketoglutaric acid and of pyruvic acid was calculated from ten collection periods.)[2] The blood was deproteinized immediately after venipuncture and the clear supernatant was processed as usual.

The values of both the α-keto-acids in blood varied during a 24-hr. period. The variations averaged ± 15 per cent in the case of α-ketoglutaric acid and ± 20 per cent of values of pyruvic acid. 1·00–2·70 mgm. of α-ketoglutaric acid per 100 ml., and 0·90–1·70 mgm. of pyruvic acid per 100 ml. of urine were usually found. (The concentration was found to be dependent upon diuresis.) Women excreted more of these acids during 24 hr. than men ; this difference being accentuated in the case of α-ketoglutaric acid (Table 1).

The mean values of clearances of endogenous α-ketoglutaric and pyruvic acids were higher in women as compared with men (Table 1). In patients with kidney damage the values of both clearances were lowered ; the lowest one was found in nephritis of middle degree.

Highest values of clearances were observed between 1 p.m. and 5 p.m., and between 7 p.m. and 9 p.m.

The cause of different concentrations of both α-keto-acids in blood and urine is to be seen in kidneys. The kidney does not only eliminate the α-keto-acids, it participates in their metabolism, too[3]. The trans-aminations, oxidative deaminations, and oxidative

Table 1. Mean Values of α-Ketoglutaric and Pyruvic Acids in Blood and Urine during 24 hr. and the Clearances in Healthy Persons, and in Patients with Kidney Damage

		No. of cases	Corresponding keto-acid	Mgm. per 100 ml. of blood	Mgm. in 24 hr. urine	Mean clearance values in 24 hr. (ml. per min.)
Healthy	women	3	*KG*	0·14 ± 0·05	18·66 ± 4·41	8·47 ± 1·86
			P	0·44 ± 0·09	11·41 ± 3·10	1·76 ± 0·43
	men	3	*KG*	0·15 ± 0·06	11·95 ± 2·52	7·67 ± 1·91
			P	0·51 ± 0·12	9·62 ± 2·67	1·46 ± 0·42
Kidney damage	women	5	*KG*	0·16 ± 0·07	17·36 ± 3·81	7·93 ± 1·66
			P	0·58 ± 0·13	11·36 ± 2·95	1·52 ± 0·39
	men	5	*KG*	0·17 ± 0·06	11·99 ± 2·16	5·80 ± 1·10
			P	0·65 ± 0·16	10·27 ± 2·15	1·30 ± 0·36

KG, α-Ketoglutaric acid; *P*, pyruvic acid.

decarboxylations will be of principal importance here. It is possible to explain the relatively high concentration of α-ketoglutaric acid in urine (almost 10 times higher than that in blood) by either its lower reabsorption in renal tubules or by its higher elimination rate in the kidneys.

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Respiratory Function of the Swim-bladder of *Notopterus* (Lacepede)

Bridge[1], working on the swim-bladder of *Notopterus borneensis* (Bleeker), and Srivastava[2], on that of *Notopterus chitala* (Buchanan-Hamilton), concentrated their attention only on the general plan of the organ.

A detailed account of the swim-bladder and its relation with the internal ear in the genus *Notopterus* has already been published by me[3]. During the course of study, the fish lived for an indefinite period in the laboratory even when the water in the aquarium became foul and contained less than 0·5 p.p.m. of dissolved oxygen for most of the time. The specimens of *N. chitala* and *N. notopterus* (Pallas) kept in the aquarium rose to the surface to gulp air at regular intervals. If they were prevented from rising they died in 4–6 hr. The duration of time between the two consecutive gulps of air varied generally from 2 to 8 min. under normal conditions. The frequency of surface visits increased after air was removed from the swim-bladder forcibly by pressing at its caudal cæcum (Fig. 1) or by drawing air out of the organ by means of a hypodermic syringe. Thus it may be presumed that a part of the air gulped by the fish enters its swim-bladder through its pneumatic duct at intervals and thus brings about a regular exchange of gases between the cavity of the organ and the exterior.

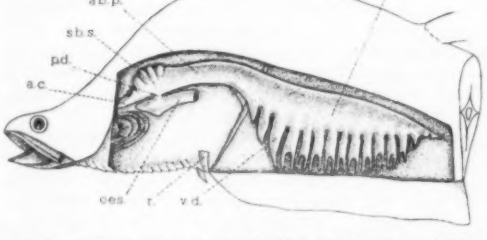

Fig. 1. Lateral view of swim-bladder of *Notopterus chitala*. *ab.p.*, Abdominal portion; *a.c.*, auditory cæcum; *c.c.*, caudal cæcum; *oes.*, œsophagus; *p.d.*, pneumatic duct; *r.*, rectum; *sb.s.*, subspherical sac; *v.d.*, ventral diverticulum

Histological study of the swim-bladder wall shows that the tunica interna is abundantly supplied with blood capillaries. The blood is brought in close contact with the contained gases which diffuse through the thin layer of epithelial cells. The circulation of blood is modified in the organ to facilitate its function as an accessory respiratory organ on the plan observed by Carter and Beadle[4]. The blood supply is from the dorsal aorta and the oxygenated blood is drained back to the heart through the posterior cardinal vein.

Further evidence of aerial respiration came from the analyses of gases from the swim-bladder of the fish. The gases were drawn from the caudal cæcum of the swim-bladder by means of a hypodermic syringe and analysed by an apparatus made in the laboratory on the plan described by Fry[5]. Immediately after *N. chitala* had gulped air, the percentages of oxygen and carbon dioxide in the gases of its swim-bladder were found to be (mean) 16 and 0·5 respectively. But when the fish were prevented from gulping air for 10 min., the percentages of oxygen and carbon dioxide in the gases of its swim-bladder were found to be (mean) 6 and 4 respectively. The water contained 1 p.p.m. of dissolved oxygen and 20 p.p.m. of free carbon dioxide during the above observations.

The air-breathing habit of *Notopterus* has not been recorded so far. Behaviour of *Notopterus* regarding its aerial and aquatic respiration under various free carbon dioxide and dissolved oxygen contents in water is being studied. Work on the physiological aspects of its aerial respiration is in progress, and a detailed account will be published elsewhere.

I am grateful to Dr. M. Chandy, under whose guidance the above work was done. Thanks are due to Prof. M. L. Bhatia, for encouragement and facilities offered in the Department.

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HÆMATOLOGY

Significance of Thrombin-E in the Prothrombin Activation Sequence

Thrombin-*E*, or esterase thrombin, is an enzyme that uses fibrin monomer and fibrin as a substrate, but not fibrinogen[1,2]. Blood does not clot in the presence of thrombin-*E*, but on the contrary there is a tendency for lysis. It is derived from prothrombin, and arises before thrombin-*C*, which is the traditional enzyme considered in the blood coagulation literature[3]. In this report we emphasize the significance of thrombin-*E* in a prothrombin activation sequence. We describe some pharmacological effects of a purified thrombin-*E* preparation, chief of which is its fibrinolytic effect upon intravenous infusion in dogs. This *in vivo* fibrinolysis is far more powerful than its *in vitro* fibrinolytic effect. These facts are consistent with previous postulations[4,5] as follows: certain chemo-receptors excite themselves with thrombin and through a reflex arc call into play a neuro-humoral mechanism involving a physiological anti-coagulating system.

Two versions of the prothrombin activation sequence have been presented, but with no greater completeness than was comprehensible in view of the available information at the time[6,7]. With the knowledge that thrombin-*E* arises before thrombin-*C* an expanded sequence can be considered. First, there is prothrombin, which is recognized as a distinct single entity on the basis of isolation work[8,9]. It may activate according to the following sequence:

Prothrombin	becomes thrombin in two-stage analytical reagents
↓	
Prothrombin derivative I	does not become thrombin in two-stage analytical reagents
↓	
Prothrombin derivative II	becomes thrombin in two-stage analytical reagents
↓	
Thrombin-*E*	uses fibrin monomer and fibrin as substrate, but not fibrinogen
↓	
Thrombin-*C*	uses fibrinogen, fibrin monomer and fibrin as a substrate
↓	
Thrombin-*E*	uses fibrin monomer and fibrin as substrate, but not fibrinogen

Thrombin-*E* can be obtained from prothrombin in several ways. For example, by activating prothrombin in calcium solutions[2], or by letting thrombin-*C* preparations deteriorate[1]. But these ways are not practicable, for some thrombin-*C* usually remains and the yields are low. Later we hope to report on the derivation of a type of thrombin-*E* obtained by activation of acetylated prothrombin. It seems to be as convenient a way as by acetylation of thrombin-*C* [10], which was the method employed to get the material for our pharmacological studies.

Having achieved the preparation of homogeneous (ultracentrifuge) thrombin-*E* [10] we were ready to see, for the first time, some of its pharmacological effects. Approximately 15 mgm., dissolved in 100 ml. physiological saline solution, were infused in the femoral vein of a dog previously given 'Nembutal' anæsthesia. The infusion lasted over a period of an hour. There were no changes in blood pressure, respiratory and cardiac rate, or temperature. At completion of the infusion blood was drawn. Sometimes it clotted and then lysed. Sometimes the fibrinogen was depleted and there was no clotting. Of the several blood analyses done it was of interest to see a decrease in platelet and white cell count, and almost a two-fold increase in blood sugar and cholesterol concentration. By the end of 24 hr. all blood values were back to normal. The profound fibrinolysis is due to physiological mechanisms activated by thrombin-*E*. The equivalent concentrations or even a hundred times more of thrombin-*E* added to dog blood in test-tubes was never followed by visible lysis. On the other hand, plasma from dogs given infusions could be mixed with a standard fibrin clot and lysis was easily measured.

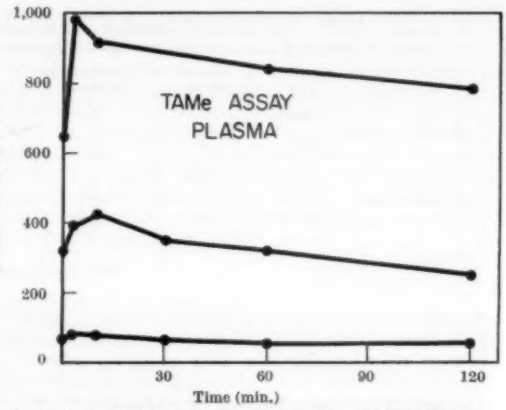

Fig. 1. Acetylated thrombin, in concentrations of 1,300, 650 and 130 units per ml., was mixed with an equal volume of defibrinated cow plasma. The activity at first increased and then declined to lower levels. The initial increase in activity was proportional to the thrombin-*E* concentration

To clarify the question of thrombin-*E* neutralization by antithrombin we made several analyses. In contrast to the rapid neutralization of the activity in thrombin-*C* [11] there seems to be an intensification of esterase activity during the first half hour after plasma is mixed with thrombin-*E* (Fig. 1). If the concentration of the latter is not too high it eventually is neutralized by antithrombin. Thus it is quite possible to have thrombin-*E* activity in the face of plasma antithrombin.

There are two facts that can be used to develop a perspective on the significance of thrombin-*E* in the prothrombin activation sequence. First, it arises before thrombin-*C*, and secondly, it activates fibrinolytic mechanisms in the intact mammal. The control of prothrombin activation is by a group of anticoagulants and procoagulants functioning in dynamic equilibrium[12]. With procoagulants gaining ascendency, thrombin-*E* can form and excite physiological mechanisms concerned with fibrinolysis. Even excess of thrombin-*E* is without danger so far as fibrinogen activation is concerned, and it is also not a catalyst for prothrombin activation[2]. However, if the prothrombin activation sequence goes farther we obtain thrombin-*C*. It can also excite fibrinolytic mechanisms[4,5], presumably through use of its thrombin-*E* component, but in 'excess' concentration it activates fibrinogen and clotting follows. Our results also account for the observed therapeutic effect obtained in cases of thrombosis where small amounts of crude thrombin-*E* preparations were infused[13]. The view that chemo-receptors react to the appearance of thrombin[4,5] focuses attention on events at an advanced stage of prothrombin activation. Already before that, thrombin-*E* can be effective, and it probably is constantly functioning to help maintain the

fluidity of the blood, for it could be present in significant concentration at all times. For example, we made a few analyses and found five units of esterase activity in dog plasma and thirteen units in 2-hr.-old dog serum. This may not have been due to thrombin, but the same method for analysis was used as is routinely employed for the measurement of thrombin-*E* activity[1,2].

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Erythrocyte Glucose-6-Phosphate Dehydrogenase-deficient Subjects : Enzyme-Level in Saliva

AN erythrocyte glucose-6-phosphate dehydrogenase deficiency has been described among Negroes, non-Ashkenazi Jews and Italians, mostly of Sardinian origin[1-3]. This enzymatic abnormality is known to be associated with an increased susceptibility to hæmolysis following ingestion of a number of drugs as well as of *fava* beans[4,5], and appears to be transmitted as a sex-linked incompletely dominant trait[6].

Recently, a low enzyme-level in the platelets, white blood-cells and liver-homogenates of affected subjects was demonstrated in our laboratory[7,8]. Marks *et al.* have also found low enzyme-levels in leucocytes of affected Caucasians in contrast to their previous reports on normal glucose-6-phosphate dehydrogenase activity in leucocytes of affected Negroes[9]. This apparent difference, in itself noteworthy, may be due to either (*a*) at least two or more independent genetic mutations, or (*b*) an effect of different genetic modifiers, which determine the degree of the enzyme defect in the population groups studied.

Since this genetic abnormality affects many primitive peoples, from whom we have had difficulties in obtaining blood, the search for other sampling methods to investigate this defect was undertaken. Saliva was found to be suitable for this purpose. Samples of it were obtained from twenty-six fasting subjects (controls), and from fourteen 'test cases', all males, deficient in glucose-6-phosphate dehydrogenase. The saliva samples were spun down at 1,000*g* for 15 min., 1 ml. of the supernatant being used for the assay. Glucose-6-phosphate dehydrogenase and 6-phosphogluconic dehydrogenase were assayed by previously described methods[8,10,11]. The enzymatic activity is expressed in units per mgm. of protein. The phosphogluconic dehydrogenase activity in enzyme-deficient individuals was not significantly different from that of normal subjects.

Table 1. GLUCOSE-6-PHOSPHATE DEHYDROGENASE (G-6-P.D.) ACTIVITY IN SALIVA OF NORMAL AND ENZYME-DEFICIENT SUBJECTS

Subjects	Number	G-6-P.D. level in units*	
		Range	Mean
Control	26	2–27	8 ± 6·3
Sensitive	14	0–1·22	0·54 ± 0·4

$$* \text{ Unit} = \frac{(OD/\text{min.})}{(\text{mgm. protein})} \times 10^3$$

As can be seen in Table 1, the level of glucose-6-phosphate dehydrogenase in the saliva of 'test cases' is significantly lower than that in normal controls, ($P > 0{\cdot}001$) thus demonstrating that saliva, which is easily obtained, is suitable for the detection of enzyme-deficient subjects.

Preliminary investigation of the skin of normal and enzyme-deficient subjects has revealed that low enzyme-levels of the latter group are also demonstrable. These findings further support our observation that the genetic enzymatic defect in our population affects all tissues, not only the blood cells.

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Inheritance of a New Group-Specific System demonstrated in Normal Human Sera by means of an Immuno-Electrophoretic Technique

IN a previous communication[1] a new group-specific system was demonstrated by means of a modified immuno-electrophoretic technique[1-3], and it has been shown that this system is not related to the haptoglobin groups[1,3]. Thus, by the content of either a fast-moving precipitating component (G.c.1), a slow-moving precipitating component (G.c.2) (Fig. 1), or a

precipitating component which gives an immuno-precipitate with two peaks, human sera can be classified into three qualitatively different groups, which have been called groups 1, 3 and 2 respectively.

It has been shown that the precipitate with two peaks, or in less optimal circumstances, a plateau-like shape, can also be obtained by mixing sera belonging to groups 1 and 3 in equal amounts and subjecting them to immuno-electrophoresis. In all these instances (7 experiments with different sera) a precipitate is obtained which is indistinguishable from the precipitating component with two peaks found in certain normal sera, which are thereby characterized as belonging to serum group 2, and from these experiments presumably contain both the fast-moving and slow-moving precipitating components (Fig. 2)[1].

These group-specific components differ from the haptoglobins by their precipitates not taking the benzidine-stain after addition of hæmoglobin, they do not show any change in electrophoretic position after addition of hæmoglobin and are further found in all human sera hitherto investigated, including a few sera which were found to lack any haptoglobin demonstrable by starch-gel and agar-gel electrophoresis[2]. The group-specific components are found in the α_2-region occupying electrophoretic positions approximately corresponding to the haptoglobins 1–1 and 2–2, when sera are investigated without addition of hæmoglobin; but they are not correlated to the haptoglobin-groups determined in 30 sera by means of starch-gel electrophoresis.

While it has not yet been excluded that these group-specific components might be identical with, for example, the post-albumins[4], the above-mentioned preliminary denotations will still be used.

In the present communication the results of a genetical study of mother–child material (kindly obtained from Prof. Birger Broman, State Institute for Blood Group Serology, Stockholm) and family material (kindly obtained from Prof. Rune Grubb, Bacteriological Department, Lund) will be given.

Family data are summarized in Table 1. They are in agreement with the interpretation that the character is monogenetically inherited and that types 1 and 3 represent the two homozygous classes and type 2 is the heterozygote.

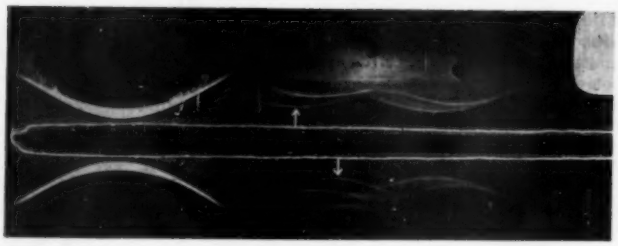

Fig. 1. Immuno-electrophoretic pattern of two normal sera characterized as belonging to group 1 (upper basin) and group 3 (lower basin). The group-specific components are indicated by arrows. To the far left, the position of albumin is shown

Fig. 2. Immuno-electrophoretic pattern obtained by mixing equal amounts of the same sera as in Fig. 1 (upper basin) as compared with a normal serum (lower basin) containing a precipitate with two peaks or at least a plateau-like form, the serum therefore characterized as belonging to group 2 or the heterozygote. A different immune serum is used from that in Fig. 1. This does not, however, affect the determination of the group-specific components

Table 1

Parental phenotypes		No. of families	No. of children belonging to type			Total
Father	Mother		1	2	3	
1	1	6	30	0	0	30
1	2	2	4	2	0	6
2	1	4	4	7	0	11
2	2	3	2	3	1	6
1	3	1	0	2	0	2
3	1	1	0	3	0	3

Table 2

	Number of individuals belonging to type			Total
	1	2	3	
Observed	161	108	23	292
Expected	158·3	113·4	20·3	292

$\chi^2 = 0{\cdot}662$, 1 degree of freedom. $P = 0{\cdot}3$–$0{\cdot}5$.

A randomly sampled specimen of mother–child material confirmed this hypothesis, in that among 76 mothers of type 1 no one had a child of type 3, and among 14 mothers of type 3 no one had a child of type 1. Gene frequencies were estimated from these data, tabulated in Table 2, using the scoring method devised by Cotterman[5] for material composed of related individuals. The frequency of the allele responsible for the fast-moving component was found to be 0·74 and the frequency of the other allele 0·26. A χ^2-test for the agreement with the postulated manner of inheritance and for genetic equilibrium was performed (Table 2). The deviations from the expected frequencies are very small and not statistically significant.

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PLANT PHYSIOLOGY

Effect of Coumarin on the Growth of *Rhodotorula rosea* Cultures

COUMARIN ($C_6H_4OCOH{=}CH$) and closely related compounds are strong regulators of the germination and growth of seedlings of different species of plants[1]; the stimulatory[2] or the inhibitory[3,4] effect depends on the concentration of coumarin and on the species of plant tested. Unfortunately, there is almost no information concerning the effect of coumarin on the growth of micro-organisms[5] and we have, therefore, carried out tests with *Rhodotorula rosea*.

Into 100 ml. Erlenmayer flasks were poured 24·5 ml. synthetic nutrient medium[6] (twice condensed), 24·5 ml. special solution of coumarin, or distilled water in the case of control, and sterilized in an autoclave. After cooling, 1 ml. suspension of *Rh. rosea* (48-hr. culture grown on sweet beer, by dilution 1 : 10,000) was added to each flask, which was then placed in a thermostat at a temperature of 27° C.

The growth of micro-organisms was measured by microscopic observations of preparations stained with methylene blue solution according to Fink and Kühles[7] in Thoma's counting chamber. Besides the whole number of cells, dead and budding cells were also counted.

The results are presented in Tables 1 and 2.

Table 1. EFFECT OF COUMARIN CONCENTRATIONS ON RATE OF GROWTH OF *Rhodotorula rosea* AFTER VARIOUS TIMES

Concentration of coumarin (p.p.m.)	Percentage of growth after (hr.) 48	72	96
0 (control)	100	100	100
1·0	81·2	72·4	64·0
10·0	152·9	112·3	78·4
100·0	77·1	53·8	36·1
1,000·0	6·4	4·6	2·0

Table 2. EFFECT OF COUMARIN ON THE DEGREE OF BUDDING AND DEAD CELLS

Concentration of coumarin (p.p.m.)	Percentage budding after (hr.) 48	72	96	Percentage dead after (hr.) 48	72	96
0 (control)	72·6	67·8	77·1	8·3	6·2	4·7
1·0	68·0	69·9	73·9	8·6	9·4	6·4
10·0	78·7	81·0	78·2	5·4	5·3	6·5
100·0	55·6	57·9	68·8	9·5	20·3	14·7
1,000·0	14·4	29·4	0	42·8	58·9	96·1

Note: all numbers are the average of 3–4 repetitions.

The results in Table 1 show that coumarin can stimulate or inhibit the growth of culture *Rh. rosea*, depending on time and concentration. At a concentration of 1,000 p.p.m. it almost totally inhibits development of the yeast: in a 48-hr. culture there are only 6 per cent of cells compared with the control; in this case 43 per cent of cells are dead. In a 96-hr. culture there are only 2 per cent, and in this case almost all cells are dead. The fact must be recognized that the cells alive in a culture such as this change very much morphologically (unpublished work).

Interesting results are obtained in cultures after adding coumarin at a concentration of 10 p.p.m. After 48 hr. in such a culture there is an increase of the whole amount of cells to the extent of 50 per cent (152–100 per cent of control); in cultures lasting 72 hr. stimulation decreases to about 12 per cent. In cultures lasting 96 hr., however, instead of stimulation, an inhibition of about 20 per cent of growth is observed. It is important that the decrease of stimulation with ensuing inhibition is proportional to the time of growing culture on nutrient medium with a supply of coumarin.

Parallel to the increase of the whole amount of cells in cultures treated with coumarin at a concentration of 10 p.p.m. there is an increase in the number of budding cells, but there is a decrease in the number of dead cells (expressed as a percentage of the whole number of cells in the given series taken as 100 per cent); by passing from stimulation to inhibition, at the same time, the increase of the amount of dead percentage of cells is observed.

An important problem is that coumarin in a concentration of 1 p.p.m. shows inhibitory action.

On the basis of the investigations described above it may be suggested that coumarin has a decisive influence on the living process of the yeasts (we obtained similar results on *Saccharomyces cerevisiae*), and it is very probable that it influences the development of other strains of micro-organisms.

We thank Prof. W. Moycho for his critical remarks made while working on this problem.

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A Reversible Inhibition of Photosynthesis in Synchronized Cultures of Algae

STEADY-STATE algal suspensions have been a favourite subject in studies of inhibitory effects of light on photosynthesis[1–5]. Light intensities several times higher than the intensity of full sunlight were often employed. The unfavourable effects of strong light were seen in the decreased photosynthetic rates[1–4] and/or in the destruction of the photosynthetic pigments[5]. A recovery process has been observed after transferring the organism into dark or to lower light intensities[2,4,5]. An emphasis on the dependence of the photo-inhibition on a very strong light has obscured the much wider nature of the phenomenon. The general employment of steady-state suspensions precluded an insight into the complexity of the situation on the cellular level.

A steady-state microbial population consists of cells of different developmental stages. Any characteristic obtained for a steady-state suspension is a statistical average from the characteristics of the individual cells and, like any average, it may or may not be intrinsic to any portion, or, strictly speaking, even to a single cell, of a given population. It has been shown that in the course of the life-cycle *Chlorella* cells pass through stages which differ in the levels of metabolic and growth activity[6–9], in the contents of cell constituents[10,11], and in the sensitivity to environmental factors[12].

The effect of light on photosynthesis in cells of different developmental stages also proved to be

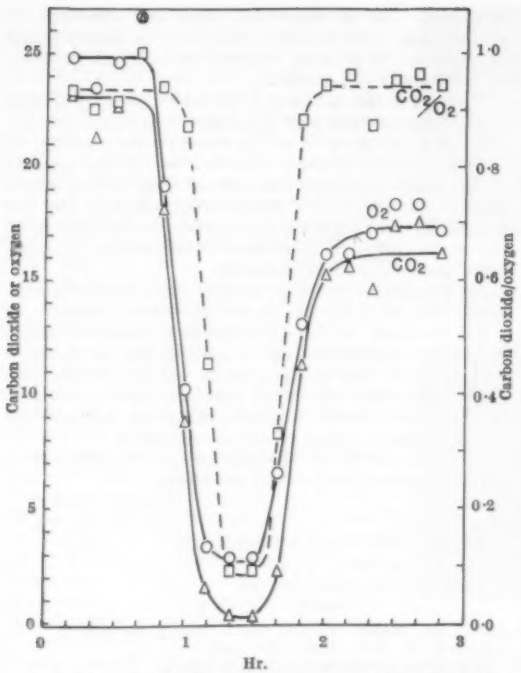

Fig. 1. Time course of the gas exchange during a photosynthetic experiment in 3-hr.-old cells of *Chlorella* 7–11–05. Carbon dioxide consumption and oxygen evolution in mm.³ of gas per mm.³ of cells per 10-min. intervals. Assimilatory quotients (carbon dioxide/oxygen) for the corresponding intervals. Note recovery of rates for all measurements

different[13]. Cells of a certain intermediate age are characterized by a higher position of the light-saturating point and by higher rates of photosynthesis at light saturation. In the course of a photosynthetic experiment these cells show a peculiar phenomenon. The rate of the gas exchange first declines; then, after reaching a low point, it increases and may eventually reach or surpass the level of the initial rate at the start of the experiment.

The results depicted in Fig. 1 were obtained with a synchronized suspension of the high-temperature strain, *Chlorella* 7–11–05[7,8]. Cells 3 hr. old were used. Studies were done with the two-vessel technique in 0·02 *M* potassium dihydrogen phosphate-suspending fluid at *p*H 4·5. Temperature during both the culturing period and photosynthesis measurements was maintained at 39° C. Illumination during photosynthesis studies was provided by incandescent lamps with the intensity at the level of the reaction vessels near 2,000 foot candles. This intensity is slightly higher than the saturating light intensity for the steady-state suspensions of this strain (near 1,600 foot candles)[14].

As seen in Fig. 1 both the oxygen evolution and carbon dioxide consumption undergo sharp declines with time. Carbon dioxide consumption is affected more than oxygen evolution and, consequently, the assimilatory quotient (carbon dioxide/oxygen) drops to a very low level. In some experiments the carbon dioxide consumption was even observed to turn into carbon dioxide evolution and the oxygen evolution into oxygen consumption.

After reaching a low level the rates of gas exchange start to rise. Eventually they may reach the initial level or even surpass it. The rate of the recovery of carbon dioxide consumption is higher than that of oxygen evolution and, as a result, the assimilatory quotient gradually rises to the initial level at the start of the experiment.

For comparison, the time course of the events in a steady-state suspension of the same strain and under similar conditions is depicted in Fig. 2. The rate of oxygen evolution declines with the time in accordance with earlier observations by Emerson[1]. Carbon dioxide consumption also shows a gradual though slightly greater decrease with time. As the result, assimilatory quotient slightly decreases during the course of the experiment. Changes in the rates of the gas exchange in the steady-state suspension are not nearly so dramatic as in synchronized 3-hr. cells and recovery of the rate does not occur.

A clue to the discrepancy in the time course of photosynthetic gas exchange in synchronized 3-hr.-old cells (Fig. 1) and in a steady-state suspension (Fig. 2) is provided by an understanding of the diversity of cellular characteristics among members of a steady-state microbial population. It will be shown in following publications that algal cells of later developmental stages have a very low if any capacity for a recovery of photosynthetic rate in the course of the experiment. The time course of the photosynthetic gas exchange in older cells would be described by a constantly decreasing rate with the slope of the curve much steeper than that depicted in Fig. 2 for the steady-state suspension. At any given time during the measurement of photosynthesis the rate of the gas exchange for the steady-state suspension is an average of the rates of cells in all possible developmental stages. The preponderance

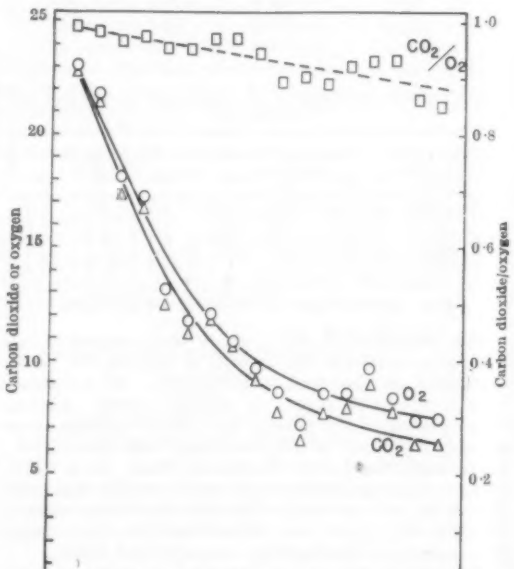

Fig. 2. Time course of the gas exchange during a photosynthetic experiment in a steady-state suspension of *Chlorella* 7–11–05. Carbon dioxide consumption and oxygen evolution in mm.³ of gas per mm.³ of cells per 10-min. intervals. Assimilatory quotients (carbon dioxide/oxygen) for the corresponding intervals. Note absence of recovery of rates

in such a suspension of older cells in later developmental stages results in a curve described in Fig. 2.

A basic observation from these studies is that the decrease in the rate of the photosynthetic gas exchange occurs at illuminance assumed to be most favourable for photosynthesis—just above light-saturating intensity. This decrease has nothing to do with the "lack of essential nutrient salts"[1] and it is not "the result of injury by the phosphate solution"[1] since the inhibition can be followed by a recovery of the rate without any apparent change in experimental conditions. The recovery of the rates is not connected with growth phenomena in the common sense of the word. Under conditions employed in these investigations, both these processes—the inhibition of photosynthesis and the increase in the rate as the result of building up some participants of the photosynthetic process—go simultaneously, the actual rate of the gas exchange being a consequence of the inter-play of these participating processes.

The magnitude of these two processes, and, therefore, the outcome of the competition between them, is greatly affected by the time factor in the course of the experiment and by the developmental stage of the cells. A resolution of the intricate intimacy of photosynthesis and development may prove advantageous in studies of both these processes.

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PATHOLOGY

Effect of Salicylate on the Activity of Plasma Enzymes in the Rabbit

ELEVATIONS of glutamic-oxaloacetic and glutamic-pyruvic transaminases have been reported to occur in sera from more than 50 per cent of children with rheumatic fever treated with either aspirin or sodium salicylate[1]. The injection of sodium salicylate in the rat caused an increased activity of xanthine dehydrogenase in the blood but a decreased activity of the enzyme in the liver, and it was suggested that the salicylate caused liver and other tissue damage leading to an increased rate of release of enzyme protein into the circulation[2]. We have therefore studied the effects of prolonged oral administration of salicylate on the activities of five plasma enzymes and on tissue histology in the rabbit.

Eight adult rabbits were given salicylate, in three divided doses each day, as either 5-grain soluble aspirin tablets B.P. or as 1 gm. per ml. aqueous solution of sodium salicylate. The aspirin tablets or the sodium salicylate solution were either placed or delivered from a syringe at the back of the animal's tongue and were readily swallowed when the mouth was then held shut. After an initial control period of two weeks, each rabbit received 0·75, 1·0 or 1·5 mgm. of the aspirin or sodium salicylate per gm. of body-weight each day for successive two-week periods. Blood specimens were collected from ear veins into heparinized containers at twice-weekly intervals and the separated plasma analysed for salicylates[3], glutamic-oxaloacetic and glutamic-pyruvic transaminases[4], *iso*citric dehydrogenase[5], lactic dehydrogenase[6] and aldolase[7]. The rabbits were killed by intravenous nembutal and portions of the liver and other tissues were removed and fixed in formol-saline for histological examination. Normal values for the activities of the five plasma enzymes in the rabbit were established by analysing random blood samples from 25 adult animals (Table 1).

Table 1. PLASMA ENZYME ACTIVITIES IN 25 CONTROL RABBITS
Results given as means and standard deviations

Enzyme	Units per ml. of plasma	Incubation temperature (° C.)
Glutamic oxaloacetic transaminase (*GOT*)	15·3 ± 4·6	37
Glutamic-pyruvic transaminase (*GPT*)	22·0 ± 8·5	37
Lactic dehydrogenase (*LD*)	5·2 ± 1·9	25
*iso*Citric dehydrogenase (*ICD*)	270 ± 90	25
Aldolase (*Ald.*)	10·8 ± 4·9	37

Increases in the activity of plasma enzymes were observed in six rabbits during the experiment, and typical results from two animals showing a marked and progressive rise in all the enzyme activities are given in Table 2.

Table 2. ACTIVITIES OF PLASMA ENZYMES IN TWO RABBITS

Day of experiment	Plasma salicylate (mgm./100 ml.)	Activity of plasma enzymes (units/ml.) *GOT*	*GPT*	*LD*	*ICD*	*Ald.*
30	52	9	12	15	280	8
32	64	11	8	34	660	6
37	78	58	18	60	820	73
40	75	203	25	132	3,200	150
19	38	5	3	4	160	9
24	52	7	4	12	170	5
27	31	26	40	12	2,600	34
29	52	780	140	32	4,000	125

It was necessary both to achieve and maintain plasma salicylate concentrations higher than 30 mgm. per 100 ml. in the susceptible rabbits to produce increased activity of plasma enzymes, and the time intervals between the initiation of salicylate administration and the first appearance of an enzyme abnormality ranged from 13 to 33 days. Histological examination revealed unequivocal signs of liver damage (cloudy swelling and fatty infiltration) in two of the six rabbits showing increased activity of plasma enzymes. The other tissues of these two

rabbits and the tissues of the remaining animals were histologically normal.

The results show that the prolonged oral administration of salicylate caused increased activity of plasma enzymes in 6 out of 8 rabbits, but this was associated with definite signs of liver damage in only 2 of the animals. It is possible that these two rabbits represent an extreme case and that the liver and other tissue damage in the remaining animals was not gross enough to be detected by conventional histological methods. Zierler[8] has observed an increased flow of aldolase across rat muscle under conditions, such as anoxia, which alter muscle metabolism and membrane permeability. Concentrations of salicylate greater than 30 mgm. per 100 ml. uncouple oxidative phosphorylation reactions in mitochondrial suspensions and in the isolated rat diaphragm[9] and thus inhibit the synthesis of adenosine triphosphate. The selective permeability of cellular membranes depends on a normal rate of production of adenosine triphosphate. The uncoupling action of salicylate may therefore affect the permeability of many tissues, leading to an increased flow of enzyme proteins into the blood without producing structural damage to the tissues of such a degree that it would necessarily be seen during the histological examination of fixed tissues.

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Intracellular Potassium in Dietary Liver Necrosis

Thin slices of liver from rats fed a normal diet (M.R.C. 41*B* cubes) lose potassium when placed in cold saline solution and re-accumulate potassium against a concentration gradient when placed in warm oxygenated Ringer solution. Mudge[1] has shown a similar sequence of events to take place in rabbit kidney slices, and Aebi[2] has shown that rat liver slices can maintain a concentration gradient between internal potassium and the incubation medium if the incubation conditions are favourable.

Dietary liver necrosis is a condition which overtakes young rats fed the diet of Himsworth[3]. The diet consists mainly of yeast and starch and is severely deficient in α-tocopherol. Liver necrosis occurs suddenly about 17 days after weaning the rats to the yeast diet[4]. Apart from mild fatty infiltration the livers are histologically normal until necrosis occurs. Feeding α-tocopherol prevents necrosis. In the present investigation liver slices from rats fed the necrogenic diet of Himsworth were found to be unable to re-accumulate potassium when placed in warm oxygenated Ringer solution after losing potassium in a cold saline solution.

Table 1. Potassium Content of Liver Slices after Incubation in the Cold for 35 min. and then in Warm Oxygenated Ringer for 60–80 min.

Diet	No. of animals	Potassium content (m.equiv./kgm. dry weight)
Stock or yeast + α-tocopherol	5	300 ± 30
Yeast diet 3–6 days	4	116 ± 13
Yeast diet 7 or more days	8	70 ± 18

Histologically normal livers from animals fed the necrogenic diet are referred to as prenecrotic livers, and the livers of animals which had been fed the diet for more than 9 days are considered as being in the late prenecrotic stage.

Pieces of liver and liver slices were dried to find water content, and then extracted with 0·15 *N* nitric acid. Sodium and potassium were measured in this extract with a flame photometer[5].

The livers of rats fed the necrogenic diet have a potassium content similar to that of livers of rats fed stock diet, or fed the necrogenic diet plus α-tocopherol. In frankly necrotic livers the potassium content is low.

Slices from prenecrotic livers and normal livers lose similar amounts of potassium when placed in a cold saline solution (sodium chloride, 150 m.equiv./l., potassium chloride, 5 m.equiv./l. at 0·5° C.). But when slices from prenecrotic livers are then placed in warm oxygenated Ringer solution they differ from slices of normal livers in showing a progressive failure to re-accumulate potassium (Fig. 1, Table 1). (Ringer phosphate, ref. 6, with 1·2 m*M* calcium and 6·6 m*M* potassium made up with water first distilled and then deionized in a 'Permutit' mixed-bed ion-exchange resin column is used as incubation medium.)

This inability is noticeable in slices from rats fed the diet for three days and becomes more severe as the time of feeding the diet increases.

The difference between slices from prenecrotic and from control livers can be detected in the first 20 min. of incubation. Slices from late prenecrotic livers

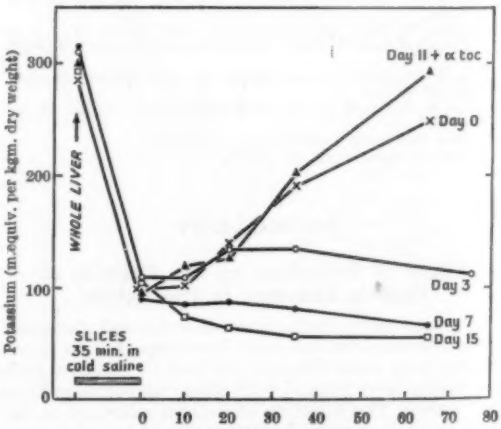

Fig. 1. Potassium accumulation in liver slices. Slices from rats fed necrogenic diet for increasing number of days. Day 11 + α-toc.: rat given 3 mgm. α-tocopherol 24 hr. before being killed. All slices kept in saline at 0° C. for 35 min. and then incubated in warm oxygenated Ringer solution

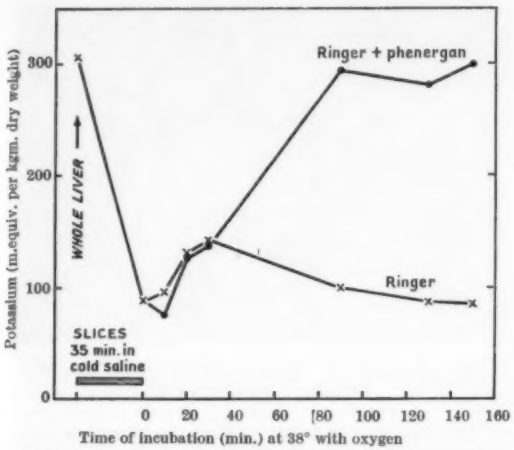

Fig. 2. Potassium accumulation in liver slices. Rat fed necrogenic diet for 5 days. Slices kept in saline at 0° C. for 35 min. and then incubated in warm oxygenated Ringer solution, with and without addition of 10^{-4} *M* 'Phenergan'

show a decline in oxygen uptake after the first 30 min. of incubation[4,7].

If a rat in the late prenecrotic stage is given α-tocopherol, liver slices taken 24 hr. later can accumulate potassium, like liver slices from rats fed stock diet, and oxygen uptake of slices does not decline. If slices from prenecrotic livers are incubated in Ringer solution containing 10^{-4} *M* 'Phenergan' (10-(2-dimethylamino*iso*propyl)phenothiazine hydrochloride), potassium accumulation is restored nearly to normal and oxygen uptake does not decline[4] (Fig. 2).

Sodium and water content of all these slices alter together and in a reciprocal manner to potassium content.

Homogenates of prenecrotic livers carry out oxidative phosphorylation with normal phosphorus/oxygen ratios.

Since the failure to re-accumulate potassium occurs in the early days of feeding the necrogenic diet, and since this failure occurs in the first 30 min. of incubation, the failure of oxygen uptake which occurs later may well be secondary to changes of electrolyte and water in the slices.

It is suggested, therefore, that these slices from prenecrotic livers probably exhibit the basic cell defect of dietary liver necrosis, namely, an inability to re-accumulate potassium once the internal cell structure has been disturbed by trauma, such as cold.

The physiological source of trauma which causes *in vivo* necrosis is being sought.

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Pathogenesis of Thrombosis

The pathogenesis of thrombosis in man is still to a considerable extent a mystery despite the considerable advances in knowledge of the subject in recent years.

In 1924 Aschoff postulated the following mechanisms as being important in intravascular clotting: (1) Changes in the coagulability of the blood, (2) changes in the formed elements, (3) changes in the blood flow, (4) changes in the blood vessels.

To these may be added several other factors more or less represented in Aschoff's scheme: the ingestion of fats[1] or alternatively essential fatty acid deficiency[2]; ageing; stress; lack of exercise; female sex hormone; tobacco smoking; operations and pregnancy. The exact importance of several of these factors is still in a good deal of doubt, however.

Changes in the coagulability of the blood have been measured by clotting time tests by several methods, by many authors, in an endeavour to determine the presence of accelerated clotting in thrombosis, with variable results. Significant shortening of the heparin plasma clotting time within 48 hr. of the onset of vascular occlusion was reported by Poller[3]. The precise relationship of such accelerated clotting to vascular thrombus formation is not established and it has been suggested that it may be, in part at least, secondary, due to the release into the circulation of coagulation products activated during clotting[4].

Studies of more specific aspects of the coagulation pattern have been performed by numerous investigators. Increases of prothrombin activity[5], factor VII [6], fibrinogen[7], antithrombin[8], thromboplastin generation[6,7] and reduced fibrinolytic activity[9] have been reported in recent thrombosis.

Changes in the formed elements have included the measurement of platelet 'stickiness', which has been found to be increased by several authors.

Changes in the blood flow have not been extensively studied owing to the difficulty of simulating events *in vivo*.

The principal anatomical vascular change predisposing to thrombosis is atherosclerosis. Duguid[10] believes organization of intra-arterial clots and fibrin deposits to be a major cause of this.

The following simple experiment may be related to the third and fourth mechanisms postulated by Aschoff[11]: 20 ml. venous blood was collected into a siliconed syringe with the minimum of hæmostasis. It was then transferred to two wax-stoppered siliconed tubes, 10 ml. being placed in each. Instead of being allowed to clot in the normal way in the rack of a water-bath the tubes of blood were transferred to an electrical blood-mixer which rotates slowly at 30 revolutions per min., imparting a slow to-and-fro motion to the blood which may simulate the pulsatile blood flow in an elastic artery like the aorta.

Under these conditions, instead of a solid clot forming, coagulation took the form of a fine deposit of fibrin on the walls of the tubes. One of the tubes was removed from the mixer after 2 hr. and transferred to a rack in a water-bath. In this a visible solid clot formed. The other tube was left in the mixer for 12 hr., but in this instance a solid clot never formed on removal to a water-bath.

If this experiment simulates at all the events *in vivo* the following conclusions may be drawn: (1) blood clotting in a major vessel with good circulatory blood flow takes the form of fibrin deposition on the walls, which supports Duguid's 'thrombogenic'

theory of atherosclerosis; (2) that a firm solid clot only forms in an artery when the local pulsatile blood flow is arrested.

The experiment is probably not related to events in venous thrombosis as the blood flow is sluggish, non-pulsatile, and atherosclerosis absent.

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ANATOMY

Marchi-Positive Bodies in Human Globus Pallidus

The Marchi method has been used extensively in this laboratory in the course of studies on degenerating nerve fibres in the central nervous system made during the past twelve years. The purpose of this communication is to report the invariable occurrence of black, Marchi-positive bodies in the globus pallidus in brains examined by this method. This is an incidental finding, unconnected with the nerve fibre degeneration under study. No previous report of it has been found in the literature.

More than 250 brains have been examined by this method. These brains came from patients dying from a wide variety of neurological and non-neurological conditions. In every brain examined there is black staining in the pallida, the amount of staining varying from brain to brain, but being approximately the same on the two sides in each brain. This black staining is in the form of rounded 'bodies' of varying size arranged in groups, frequently consisting of one or two larger 'bodies' surrounded by a number of small 'bodies'; their diameter varies from 1μ to 60μ (Figs. 1 and 2). The 'bodies' are not intracellular and are not enclosed within the sheaths of nerve fibres. Their appearance is the same in horizontal, oblique and coronal planes of section.

Sections from blocks next to those prepared by the Marchi method have been stained by the usual variety of neuro-histological methods to show changes in neurones, nerve fibres and glia. A few pink 'droplets' have occasionally been seen in sharlach *R* preparations which might be the equivalent of some of the Marchi-stained 'bodies', but otherwise no such 'bodies' have been seen in sections stained by any other method.

The purpose of the Marchi method is to demonstrate the presence of degenerating myelin. The essential mechanism in the method is the reduction of osmium tetroxide to osmium dioxide, which is black. Both normal and degenerating myelin cause this reduction; but it is inhibited in normal myelin by the addition of potassium dichromate or chlorate

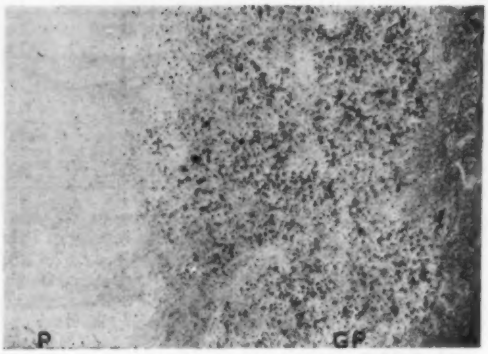

Fig. 1. Marchi preparation of putamen (*P*) and globus pallidus (*GP*) from normal brain, showing black, Marchi-positive 'bodies' in globus pallidus (× c. 13·5)

to the osmium tetroxide. Thus, in principle, only degenerating myelin stains black. In practice, artefacts of various kind may occur with this method. It must be stressed that the 'bodies' now described are completely unlike any of the artefacts ever seen, and that they are completely unlike any form of black staining in the central nervous system known to be associated with the degeneration of myelinated nerve fibres.

These bodies have a constancy of 'structure' which makes recognition of the globus pallidus easy even in tiny pieces of basal ganglia. No such 'bodies' have been found in the putamen, but very occasionally a very small number are present in the adjoining part of the internal capsule and/or in the more cranial part of the substantia nigra.

Various factors have been considered with reference to the occurrence and number of the 'bodies'. More than 250 brains have been examined by the Marchi method. Neoplastic disease, most frequently of the pelvic organs, was the most common cause of death, but brains from patients who died because of cardiac disease, of various forms of accident with and without head injury, pneumonia, tuberculosis, poliomyelitis, polyneuritis and different degenerative diseases of the nervous system were all examined. As mentioned already, the 'bodies' in the globus pallidus varied in number from brain to brain, but there were some present in all brains. No correlation could be established between the cause of death and the abundance

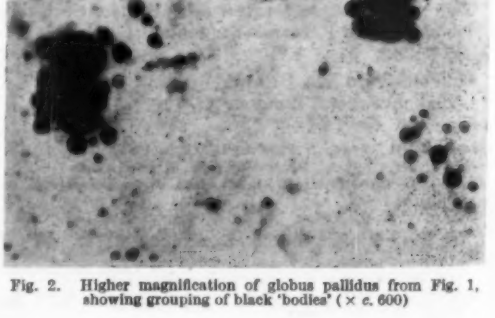

Fig. 2. Higher magnification of globus pallidus from Fig. 1, showing grouping of black 'bodies' (× c. 600)

of the 'bodies'. Similarly, no correlation could be established between the age of the patients, which varied from 20 to more than 70 years, and the number of the 'bodies'.

Although unlikely, the question might be raised whether the post-mortem treatment of the brains might have something to do with the occurrence and number of the 'bodies'. The interval between death and post-mortem varied from 2 hr. to 3 days. As the brains came not only from this hospital but from many other hospitals throughout the country, the possible effect of variations in the techniques of examination and of fixation can be excluded. No correlation could be established between the interval between death and fixation and the number of the 'bodies'.

The brains from a few species other than man have been examined by the Marchi method. These came from rhesus monkeys, cats, horses, sheep, guinea pigs, rats and mice. In none of these brains were any of these 'bodies' seen. However, the number of animals examined was too small for any definite conclusion to be drawn about the absence of these 'bodies' in mammals other than man.

At present no conclusion as to the nature of these 'bodies' is possible; but it is tentatively suggested that they may indicate some biochemical feature characteristic of the globus pallidus which has not yet been identified. Much interest is now focused on the basal ganglia. It is possible that with increasing knowledge of this region the significance of the findings reported here will become recognized.

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BIOLOGY

Dorsal Fontanelles in Selachian Neurocrania

SINCE the classical work of Gegenbaur[1] and Parker[2] the anterior opening lying on the dorsal surface of the selachian neurocrania is generally termed 'anterior fontanelle' in spite of the fact that it is different in its morphological significance and relations in different selachians. In some forms, posterior to this fontanelle, a small opening, the epiphysial foramen, is found; and in others another fontanelle, which is generally termed the 'supracranial fontanelle', appears. The study of several species of several families of Selachii showed that it is of great importance to name such fontanelles according to their morphological relation with the cranial cavity.

In *Squalus blainvillii* the fontanelle lies beyond the morphological anterior wall of the cranial cavity and represents the dorsal opening of the cavum præcerebrale found inside the spout-shaped rostral cartilage, and is accordingly named the precerebral fontanelle. Posterior to this fontanelle a small epiphysial foramen occurs. In *Squatina oculata* the fontanelle is completely supracranial, as the morphological anterior wall of the cranial cavity extends to its anterior margin. Behind it is a small epiphysial foramen. In *Triaenodon obesus* the brain extends anteriorly beyond the posterior edge of the fontanelle and thus it can be differentiated into two morphologically different parts: the anterior supracranial fontanelle lying above the cranial cavity, and the precerebral fontanelle representing the dorsal opening of the cavum præcerebrale enclosed between the three rostral cartilages. In *Torpedo sinus* the fontanelle is morphologically similar to that of *Triaenodon*, and posterior to it lies the epiphysial foramen. In *Raja batis* there are two large fontanelles separated by a narrow cartilaginous bridge. The anterior is differentiated into a precerebral fontanelle leading to the cavum præcerebrale inside the rostral cartilage, and an anterior supracranial fontanelle. The posterior is completely supracranial and is, here, termed the posterior supracranial fontanelle to differentiate it from the anterior one. In *Taeniura forskali* is found only one large fontanelle, which is completely supracranial, and termed the supracranial fontanelle.

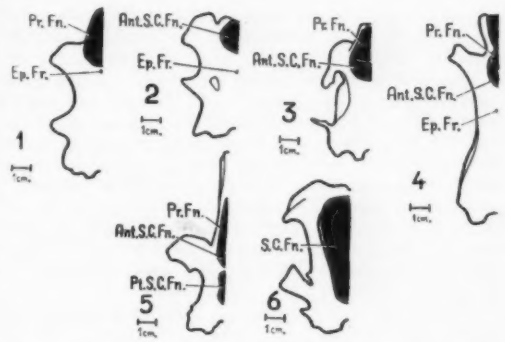

Fig. 1. Dorsal view of the neurocranium of: 1, *Squalus blainvillii*; 2, *Squatina oculata*; 3, *Triaenodon obesus*; 4, *Torpedo sinus*; 5, *Raja batis*; 6, *Taeniura forskali*. *Ant.S.C.Fn.*, Anterior supracranial fontanelle; *Ep.Fr.*, epiphysial foramen; *Pr.Fn.*, precerebral fontanelle; *Pt.S.C.Fn.*, posterior supracranial fontanelle; *S.C.Fn.*, supracranial fontanelle

Such comparative study of the dorsal fontanelles in different selachian neurocrania shows that when rostral cartilages are not present the fontanelles are morphologically supracranial as in the case of *Squatina* and *Taeniura*. In cases where rostral cartilages are present a precerebral fontanelle is represented, and it may be the only fontanelle present as in *Squalus*, or it may be confluent with a supracranial fontanelle as in *Triaenodon*, *Torpedo* and *Raja*. This view can be substantiated by the embryological work of El-Toubi[3] and Hamdy[4], who show that the single, spout-shaped rostral cartilage develops from three strips of cartilage having the same relations as the triradiate rostral cartilages. Thus it is easy to homologize the whole fontanelle in *Squalus* with only the precerebral fontanelle in *Triaenodon*, *Torpedo* and *Raja*; the anterior supracranial fontanelle in *Triaenodon*, *Torpedo* and *Raja* with that of *Squatina*; and the whole fontanelle in *Taeniura* with both the anterior and posterior supracranial fontanelles in *Raja*, being confluent with each other in consequence of the absence of the cartilaginous bridge separating them in the latter fish.

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Spore Release in *Peronospora tabacina* Adam.

Downy mildew or blue mould of tobacco caused by *Peronospora tabacina* Adam. is destructive in the American and Australian regions and has now been reported for the first time in Europe[1]. It survives in association with over-wintering or over-summering host plants of which infected *N. tabacum* is of major importance[2,3]. Such plants produce conidia that are airborne and can establish infection in distant areas[2].

De Bary suggested that dissemination of conidia of *Phytophthora infestans* (Mont.) de B. was brought about by changes in humidity causing violent movement of conidiophores and conidia were "thrown off in every direction"[4]. Ingold[5] did not agree with de Bary's conclusion; but Pinckard[6], working with *Peronospora tabacina*, supported it and also reported "ejection of sporangia (conidia) from their sterigmata by energy applied at the point of sporangial attachment". Hirst[7] concluded that sporangia (of *P. infestans*) were not removed by wet or dry gales but were dislodged by wetting, rapid changes in relative humidity and strong light. All investigators associated conidiophore movement with an increasing or decreasing relative humidity and spore dissemination with decreasing humidity. Cruickshank[8] reported intensity of spore discharge in *P. tabacina* with change in relative humidity and mechanical shock. In the experiments reported here, factors other than ambient relative humidity were also concerned in spore release.

Dissemination of conidia was investigated at Canberra, Australia, with the aid of a spore trap[9] operated among tobacco plants showing heavy sporulation. In three seasons of field experiments, the number of conidia trapped each hour of the day increased to a maximum between 0930 and 1100 hr. for periods of 12–16 consecutive days. This daily cycle was not interrupted by overnight relative humidity too low for sporulation, the conidia disseminated having been produced at an earlier date. Thus spore release was not conditional on a decreasing humidity being preceded by overnight saturation. This conclusion was confirmed by glasshouse tests in which the relative humidity subsequent to sporulation was maintained at low levels for long periods (Table 1 and Fig. 1). The results of numerous tests show that the number of days in the daily cycle of spore release was least when there was a wide range, and repeated sudden fluctuations, in temperature and humidity. Daily periodicity for 4–10 days was common.

Table 1. Relative Humidity during Consecutive Days and at Times when Numbers of Conidia Trapped were Increasing

Time of rise in numbers of conidia trapped (hr.)	Relative humidity (per cent)*			Period of test (consecutive days)
	Means at hours in first column	Actual maximum and minimum for total period of days		
		Max.	Min.	
0712–1300	61·8–63·4	74	55	10†
0712–1112	57·0–48·2	79	42	5
0815–1045	47·5–42·5	59	37	4
0745–1120	51·2–51·0	60	37	4
0645–0930	57·5–57·2	68	51	4‡

* From hygrographs among sporulating plants.
† Shaded glasshouse.
‡ Also shown graphically.

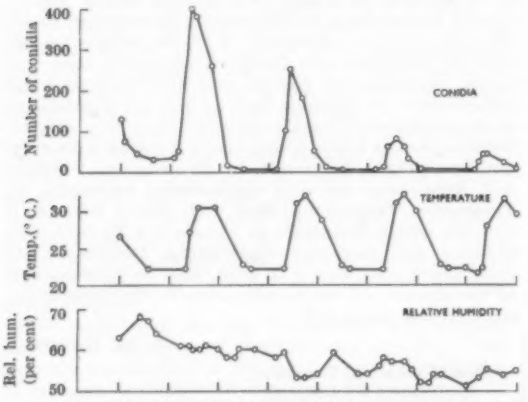

Fig. 1. *Peronospora tabacina* of tobacco. Daily cycle of spore discharge under continuous low relative humidity. Plants under low humidity from 0900 hr. of day 1. Sunrise, 0700 hr.

Examination of the fruiting structures of the pathogen *in situ* showed that twisting movements of the conidiophores were due to loss of turgidity in the stalk. This was followed by collapse of the branched superstructure, with many conidia still attached to it, on to the leaf surface. Spore release ceased but was resumed from both living and dead leaves on the same or succeeding days following periods of high ambient humidity. The spore trap data also showed that rising temperature, or light following a period of darkness, were associated with spore release. Collapsed conidiophores with attached conidia remained in that state, subsequent movements being restricted to some of the branches. The only method of spore dispersal that occurred either with or without conidiophore movement was, as described by Pinckard, due to "energy applied at the point of attachment".

These results show that spore release is regulated to provide for dissemination at intervals in time. Factors that appear to be responsible for spore release—reduction in relative humidity, increase in temperature, or light—could cause humidity or temperature-humidity changes in the region occupied by the conidiophores and thus ensure a progressive release of conidia. Whatever the mechanism involved, the results clearly show that spore discharge is a response to stimuli repeated at intervals, and that the normal interval was approximately 24 hr. Under this arrangement, conidia were held ready for dispersal and could take advantage of favourable conditions occurring at any time over a period of days following their production.

A full account of the work will be presented elsewhere.

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The Lungworm *Protostrongylus rufescens* in Australia

Of the lungworms described from domestic sheep only two, namely, *Dictyocaulus filaria* and *Muellerius capillaris*, have been identified in Australia[1], despite careful searching in the eastern States[2]. On one occasion a single larva of *Protostrongylus* spp. was found in fæces of a sheep in Tasmania (Gordon, H. McL., personal communication), but earlier records of the adults are regarded as mistaken[1,2].

P. rufescens has now definitely been identified in lungs of sheep from Millicent, in the south-eastern part of South Australia, and its larvæ in fæces from the flock. Larvæ have also been found in the abomasal contents of a sheep from Kojonup in the south-west of Western Australia. The indications from the large numbers of adults recovered (up to 600 in a single sheep) are that the worm is by no means rare in the south-western part of Australia.

The anatomy conforms in detail with that described by Gerichter[3] except that the local adults, eggs and first-stage larvæ are rather smaller; for example, males are 18–30 mm. and females 28–45 mm. long, against Gerichter's 22–46 mm. and 30–65 mm. respectively. Other authorities[4] record dimensions comparable with our measurements.

The surface of the affected lungs showed scattered yellowish grey consolidated patches of irregular shape, 3–15 mm. in diameter, identical with those described by Kassai[5]. The worms were found mostly in clumps of up to ten, obstructing bronchioles, with some lying in larger air-vessels. A rapid and highly effective method of extracting the worms is to fill the trachea and bronchi with saline, tip up and down several times, pour out, and repeat the process a number of times.

The material from Kojonup was kindly made available by Dr. I. W. Parnell, of Perth. We wish to thank Mr. A. W. Banks for advice in connexion with this work.

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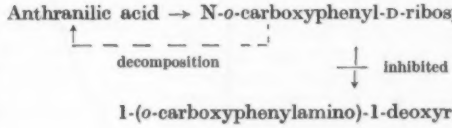
MICROBIOLOGY

Feedback Control of Tryptophan Biosynthesis

Microbiologists are becoming increasingly interested in the regulation of biosynthesis. There has been a number of reports of normal metabolites inhibiting the action of enzymes necessary for their own biosynthesis[1–6], and others of the inhibition of enzyme formation or activity[7–9]. Umbarger[1,2] has called this type of inhibition 'negative feedback'.

In this laboratory we have been interested in tryptophan biosynthesis, particularly the identification of intermediates in the conversion of anthranilic acid to indoleglycerol phosphate[10]. Moyed and Friedman[6] have recently demonstrated that tryptophan can inhibit the metabolism of anthranilic acid by a cell-free preparation of *Escherichia coli*, and considered that the site of inhibition was the condensation of anthranilic acid with 5-phosphoribosyl-1-pyrophosphate. We considered that this interpretation was premature, since the preparation could carry out more than one step and because N-*o*-carboxyphenyl-D-ribosylamine, the unphosphorylated form of the postulated condensation product, is chemically unstable at biological *p*H (ref. 10 and unpublished work by Doy, C. H.). It seemed to us that the site of inhibition might equally well be the Amadori rearrangement step:



In any event we suspected that anthranilic acid was only formed by the appropriate tryptophan auxotrophs of *Aerobacter aerogenes* and *Escherichia coli* in the absence of growth.

We have now shown (Fig. 1) that *Aerobacter aerogenes* mutant strain *NCW-T-17A*, able to respond to indole, but not anthranilic, acid and known to accumulate anthranilic acid in washed-cell experiments with minimal substrates, does not excrete detectable amounts of anthranilic acid until growth on limiting L-tryptophan has ceased. The coincidence of end of growth and the onset of accumulation suggests that tryptophan is able to inhibit a process necessary for the biosynthesis of its own precursor anthranilic acid. Because there was no lag between end of growth and the excretion of anthranilic acid, the inhibition is likely to be on the action of an enzyme rather than on enzyme formation. This conclusion is supported since cells harvested during growth, washed to remove tryptophan and then transferred to minimal substrate, immediately begin to form anthranilic acid (Fig. 2, but note tendency for acceleration). In fact, they form the intermediate at a faster rate than that observed after growth (Fig. 1). This is probably because the fresh substrate represents a condition closer to the optimum.

The conclusion that tryptophan is able to control its own biosynthesis by inhibiting the action of an enzyme necessary for a stage prior to anthranilic acid suggests that the inhibition reported by Moyed and Friedman[6] is not the earliest site of action and is therefore more of a potential control point than a real one. Since nothing is known of specific tryptophan precursors prior to anthranilic acid, the inhibition now reported makes this part of the pathway particularly important. Because of this lack of knowledge it is also necessary to have reservations about the role of anthranilic acid, since the 'natural' condensation of 5-phosphoribosyl-1-pyrophosphate may be with a compound other than anthranilic acid[11].

Tryptophan auxotrophs grow well if supplied with L-tryptophan, which suggests that tryptophan does

not inhibit the biosynthesis of precursors which it shares in common with phenylalanine and tyrosine. It is likely that, as with other examples[2,4], the 'end product' will be found to inhibit the earliest step specific to its own biosynthesis.

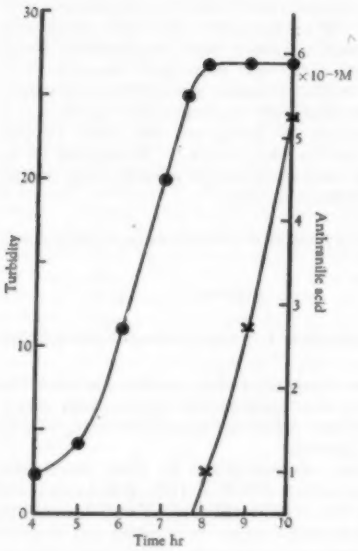


Fig. 1

Fig. 2

Fig. 1. Growth of tryptophan auxotroph *Aerobacter aerogenes NCW-T-17A* compared with excretion of anthranilic acid. Minimal substrate, 15 ml. (disodium hydrogen phosphate, 12·8 gm.; potassium dihydrogen phosphate, 2·72 gm.; ammonium chloride, 5·4 gm.; D-glucose, 36 gm.; magnesium sulphate, 10^{-1} *M*, 2 ml.; made up to 2 l., *p*H 7·7) supplemented with 2×10^{-5} *M* L-tryptophan, was lightly inoculated with the test strain and shaken in a Δ-tube at 37° C. Samples were taken for turbidity measurements (625 mμ filter, 20 = 0·6 mgm. dry wt./ml.) and determination of anthranilic acid by the method of Bratton and Marshall (ref. 12) (slightly less than 10^{-6} *M* was detectable). ●, Growth (turbidity); ×, anthranilic acid; none was detected until 8 hr.

Fig. 2. Growing cells (Fig. 1) harvested at turbidity 20, washed and resuspended in minimal substrate to equivalent turbidity, then shaken in Δ-tube at 37° C.

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Growth of Iron Bacteria in Crude Tar

In continuous distillation units of the Midland Tar Distillers, Ltd., in which vertical retort gas tar was distilled, it was found that certain heat exchangers pre-heating the crude tar became rapidly choked with deposits of fibrous material. It was at first thought that this was adventitious material such as asbestos or vegetable fibres present in the crude tar feed with entrained particles of solid material. The crude feed was, however, continuously filtered through a 'Rotoclene' filter with a clearance of ten-thousandths of an inch and examination of the material held back by this filter did not resemble the deposit within the heat exchanger. It was this fact, together with the quantity and consistent appearance of the deposit at one point in the heat exchanger train, that suggested, in fact, it was essentially a growth in the tar medium.

The fibrous matter in the deposit was demonstrated to be neither asbestos nor vegetable, and an analysis of the ashed deposit showed it to consist mainly of iron oxide and manganese salts. Under the microscope, iron oxide skeletons were readily discernible among the ash, which suggested that the deposit may at least in part have been due to biological growth. The ash was also strongly paramagnetic, which lent weight to this view, as the production of a magnetic form of iron oxide is characteristic of the activity of iron bacteria.

Samples of a freshly collected deposit were examined under the microscope. Dense populations of motile bacilli and cocci were observed, and, in addition, what appeared to be fungal filaments with multi-cellular structure with branching and spores at the branch ends were also noted. The diameter of the fibres was about 20 microns, which although larger than that of most observed filamentous bacteria, is still within the range of size of filamentous bacteria.

The suggestion, therefore, was that the prime reason for the formation of the deposit was the development of iron bacteria. Conditions in the heat exchanger were favourable for the growth of diverse species of micro-organisms. The temperature-range over the section in which the deposit was prevalent was 30–70° C.

When the quantity of iron present in the deposit was considered, it did not seem reasonable that this iron was a result of corrosion, because gross corrosion of the heat exchanger was not taking place. It seemed more reasonable to assume that the iron oxides had come from a concentration of the soluble iron salts present in the crude tar either by biological activity or purely physical and chemical means.

The deposit also contained 3·0 per cent (w/w) of sulphides, and as only a trace of sulphur was

present in the crude tar feed (as thiosulphates, thiocyanates, sulphates), here again was a process of concentration to be explained either by biological or physical and chemical means.

The mild conditions in the heat exchangers and the significant temperature-range (30–70° C.) pointed to biological activity as the prime cause of the deposit.

The cultivation of iron bacteria outside their normal environment is difficult, but a reasonable amount of 'fibrous' organism was grown on a solid medium which included an aqueous extract of the deposited material. Although the filaments could not be positively identified, their appearance agreed with descriptions found in the literature of some of the iron bacteria. They did resemble the fibres actually present in the heat exchanger deposits, so far as magnetic properties, appearance and sulphide content were concerned.

It is possible that the small motile vibrio type of organisms observed under the microscope in fresh samples were sulphate-reducing bacteria, but this has not yet been confirmed.

I wish to thank Dr. N. J. Cartwright and Mr. F. W. Moore, of the Department of Bacteriology, University of Birmingham, for their interest and assistance on the microbiological side.

P. H. Garnett

The Midland Tar Distillers, Ltd.,
Four Ashes, Nr. Wolverhampton,
Staffs.

Observations on the Nagler Reaction of some *Clostridia*

Nagler[1] showed that the surface of colonies of *Clostridium oedematiens* type *A* growing on egg-yolk – sheep-blood agar, is covered by a pearly layer. Subsequent investigations by McClung *et al.*[2] and McClung and Toabe[3] showed that this phenomenon was not restricted to *Cl. oedematiens* type *A*, but was also shown by all types of *Cl. botulinum* and by *Cl. sporogenes*, and was more evident if the blood was omitted from the medium. All the *Clostridia* which show this pearly layer on egg-yolk agar also produce an opalescence within the medium, somewhat similar in appearance to that produced by anaerobes such as *Cl. welchii* and *Cl. bifermentans*, which produce lecithinase. Oakley *et al.*[4] showed that cultures and culture-filtrates of *Cl. oedematiens* type *A* produce two distinct types of opalescence in egg-yolk emulsions: a diffuse opalescence due to a hæmolytic lecithinase (*Cl. oedematiens* γ-toxin), and a more confined opalescence due to a lipase (*Cl. oedematiens* ε-antigen). They suggested that the pearly layer also produced by *Cl. oedematiens* type *A* might be caused by the lipolytic ε-antigen (see also ref. 5). Sussman (personal communication) showed that cultures of *Cl. sporogenes* were lipolytic when grown on tributyrin agar ('Oxoid'), and that this organism developed a pearly layer when grown on an agar medium containing triolein.

The present communication presents briefly the results obtained in a study of the pearly layers produced by *Cl. sporogenes*, all types of *Cl. botulinum* and *Cl. oedematiens* type *A*.

A number of clostridia were examined for lipolytic activity by growing them as surface cultures on tributyrin agar ('Oxoid') enriched with 5 per cent of Fields's extract of red cells. Lipolysis, indicated by the development of zones of clearing in the medium about areas of growth, was shown by strains of *Cl. sporogenes*, all types of *Cl. botulinum* and *Cl. oedematiens* type *A*, but not by strains of *Cl. bifermentans*, *Cl. welchii* (types *A–F*), *Cl. histolyticum* or *Cl. oedematiens* type *B* (see Table 1). Thus, of the species examined, only those which produce a pearly layer on egg-yolk media showed lipolytic activity on tributyrin agar.

Table 1. Action of Some *Clostridia* on Media with and without Lecithin and Fat

Organism	Clearing on 'Tributyrin' agar	Egg-yolk agar		Cream-milk agar		Fat-free milk agar	
		Opal.*	Pl.†	Opal.	Pl.	Opal.	Pl.
Cl. welchii (*A–F*)	–	+	–	–	–	–	–
Cl. bifermentans	–	+	–	–	–	–	–
Cl. histolyticum	–	–	–	–	–	–	–
Cl. botulinum (*A–F*)	+	+	+	+	+	–	–
Cl. sporogenes	+	+	+	+	+	–	–
Cl. oedematiens, type *A*	+	+	+	+	+	–	–
Cl. oedematiens, type *B*	–	+	–	–	–	–	–

* Opal., opalescence. † Pl., pearly layer.
+ or –, present or absent, respectively.

The various organisms were then cultured on egg-yolk agar, full-cream-milk agar and fat-free-milk agar. The results, which are summarized in Table 1, show that all the lipolytic organisms examined produced an opalescence and a pearly layer on fat-containing media, but not on the fat-free medium. Lecithinase activity was shown only on egg-yolk agar.

Egg-yolk agar plates, full-cream-milk agar plates and fat-free-milk agar plates were spotted with pancreatic lipase (Light and Co.) and incubated at 37° C. The egg-yolk and cream plates developed zones of opalescence covered by a pearly layer, similar in appearance to those produced by the lipolytic *Clostridia*. No opalescence or pearly layer was produced by pancreatic lipase on the fat-free medium. These plates, and all the plate cultures of the anaerobes, were flooded with a saturated solution of copper sulphate, allowed to stand for a few minutes, and then rinsed with water (the copper soap test for lipase). Positive results, shown by the appearance of bluish-green zones of precipitate in the medium, were given by the egg-yolk and cream plates treated with pancreatic lipase, and by all the cultures of *Clostridia* growing on egg-yolk and cream agar and producing a pearly layer. Negative results were given by cultures not associated with a pearly layer.

These results indicate that the pearly layer and opalescence produced on egg-yolk and other fat-containing media by the *Clostridia* examined are due to lipolytic activity, and probably consist of free fatty acid. No pearly layer is produced on tributyrin agar by lipolytic organisms because the products of lipolysis (glycerol and butyric acid) are soluble. Macfarlane suggested[6] that *Cl. oedematiens* type *D* (*Cl. hæmolyticum*) may produce traces of a lipase. This organism has not been studied in the present investigation.

If the conclusions drawn are correct, it seems likely that the butyrous scum which sometimes develops on the surface of cooked-meat broth cultures of *Cl. botulinum* and *Cl. sporogenes* consists of fatty acid liberated by lipolysis. Further, the absence of a lipase from cultures of *Cl. welchii* provides an explanation for the characteristic fatty appearance of the

œdema fluid produced in pure *Cl. welchii* gas gangrene.

Further investigations along these lines are at present being made and will form the basis of a subsequent more detailed communication.

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Survival of Bacteria on Drying in Sugar/Protein Mixtures

In an investigation of the protection afforded by various sugars in the preservation of the viability of dried cultures, Hellier[1] directed attention to the advantage of a sucrose/peptone mixture over either sucrose or peptone alone. In 1951, Fry and Greaves[2] proposed their *mist. desiccans*, a serum/broth mixture containing 7·5 per cent glucose, and this has come into extensive use as a medium in which to dry a wide variety of organisms with a high retention of viability. In general, in the presence of either sugar or protein alone, the percentage survival is relatively poor; only in a mixture of the two in suitable proportions and in adequate concentration is a high degree of viability retained after drying and reconstitution. The underlying action of such mixtures has not hitherto been satisfactorily explained.

The concept of a bacterial cell as confined by a thin plasma membrane supported by an outer, stronger and more permeable cell wall is now well established, and the phenomenon of plasmolysis as displayed by various Gram-negative organisms on exposure to solutions of electrolytes and sugars such as glucose or sucrose has long been recognized as the result of the collapse of the plasma membrane due to osmotic forces caused by these substances, to which only the cell wall is permeable. During such plasmolysis the overall shape of the cell as defined by the cell wall is still clearly seen.

By the use of a micro-culture chamber[3] we have observed that cells of *Bacterium coli* dried in various sugar solutions, or even after exposure for some time to their concentrated solutions, exhibit, on returning to ordinary growth media such as broth or peptone water, a high proportion of spherical forms or protoplasts resulting from the rupture of the cell wall by the high diffusion pressure set up by the sugar temporarily trapped between the cell wall and plasma membrane. This cell wall damage can be to a large extent averted and the normal morphology and viability retained if the sugar-treated cells are returned to normal media gradually through progressively decreasing concentrations of sugar. We have evidence to suggest that the main function of the sugar in preserving viability on drying lies in its ability to preserve the cell wall intact.

The cell wall, though permeable to mono-, di- and tri-saccharides, is impermeable to proteins and to partially hydrolysed proteins such as constitute a proportion of broth, peptone, etc. By measurements of cell volume we have been able to show that the relatively mild osmotic forces exerted by such substances of higher molecular weight against the cell wall cause its contraction against the plasma membrane and thereby reduce the volume between the two. Thus, when organisms are dried in a mixture of suitable high and low molecular weight components in adequate concentration, the latter will afford protection to the cell wall on drying while the former will limit the amount of the low molecular component inside the cell and thereby reduce the risk of cell wall rupture on reconstitution.

A more detailed account of this work will be published.

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GENETICS

Effect of Selection on the Frequency of Genotypes determining Incompatibility in *Prunus avium*

An analysis of the frequency of alleles at the 'S' locus[1] in cultivars of *Prunus avium* indicated that the S_3 allele possessed a selective advantage. Since gametic selection does not appear to operate in this material, and since heterozygosity at the S locus is obligatory, it is of interest to inquire whether selection favours certain genotypes showing inter-allelic interactions, quite apart from the individual alleles they contain. In the absence of genotypic selection, the expected number of varieties of the type S_iS_j is of the form m_im_j. Calculation of an exact value of P for the actual frequencies (Gale, J. S., unpublished work) of the various genotypes is impossibly laborious, but it is possible to set an upper limit to the probability of obtaining by chance a fit as bad as, or worse than, the one observed.

If a_{ij} is the number of varieties of the type S_iS_j, the probability of getting the observed result is:

$$\frac{\dfrac{65!}{\pi(a_{ij}!)}\ \pi\left(\dfrac{m_im_j}{65}\right)^{a_{ij}}}{\sum\limits_{\text{all cases}} \dfrac{65!}{\pi(a_{ij}!)}\ \pi\left(\dfrac{m_im_j}{65}\right)^{a_{ij}}} = \frac{C}{\sum\limits_{\text{all cases}} C}$$

where $C = \dfrac{1}{\pi(a_{ij}!)}$ and summation is over every way of filling the table, given[1] $a_2 = 42$, $a_1 = 32$, $a_3 = 25$, $a_4 = 15$, $a_5 = 9$ and $a_6 = 7$, where a_i is the observed number of S_i alleles. If C_0 is the value of C for the observed case:

$$P = \frac{\sum\limits_{C \leqslant C_0} C}{\sum\limits_{\text{all cases}} C}$$

and it can be shown (Gale, J. S., unpublished work) that $\sum\limits_{\text{all cases}} C = 337{,}850{,}000\ C_0$ and that the number of cases is 3,693,833, so that $\sum\limits_{C \leqslant C_0} C$ cannot exceed 3,693,833 C_0 and

$$P \leqslant 1{\cdot}0933 \text{ per cent}$$

This upper limit of probability strongly suggests that the observed frequency can be attributed to selection operating on the genotype, and that certain combinations of alleles, in particular S_1S_3, S_2S_3 and S_1S_2, have been favoured in the course of the improvement of the sweet cherry.

Irrespective of whether this effect is due to inter-allelic interactions, or whether more extensive chromosome regions are involved, its significance for plant breeding is obvious. Furthermore, this result clearly demonstrates the response to selection of characters that might otherwise be classified as neutral to the forces operating, and underlines the importance of selection pressure[2] as opposed to genetic drift[3] in determining the frequency of Mendelian characters.

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Chromosomes of South American Amphibians

THE amphibian anurans constitute very interesting material, not only for the cytogenetic study of the evolutionary mechanism of sex determination, but also because they offer prospects from the evolutionary, phylogenetic and cytotaxonomic points of view.

South American species offer a wide scope for investigation due to their abundance and their distribution in different geographical regions of the Continent.

The only species which have been studied up to the present are: *Bufo arenarum* (Hensel)[1] and *Dendrophrynicus stelzneri*[2] which are representatives of the families Bufonidae and Brachycephalidae respectively.

With the view of extending this investigation, we have studied other species belonging to different families (Table 1).

Table 1

Species	Family	Diploid No. (2n)	Type of chromosomes
Bufo d'orbignyi	Bufonidae	22	Metacentrics
Odontophrynus americanus	Ceratophrydae	42	Metacentrics
Ceratophrys ornata	Ceratophrydae	88, 92, 98, 108	Metacentrics
Leptodactylus ocellatus	Leptodactylidae	22	Metacentrics
Pseudopaludicola falcipes	Leptodactylidae	22	Metacentrics
Pseudis paradoxa	Pseudidae	22	Metacentrics
Hyla raddiana raddiana	Hylidae	24	Metacentrics

Hyla raddiana raddiana presents, during the first meiotic metaphase, a differential bivalent, that differs from the rest of the autosomes, and is similar to that described in *Bufo arenarum* by one of us[1]. We did not attribute the characteristics of sex chromosomes to their bivalent as Yosida does[3] in a recent paper. The most remarkable fact observed by us is the high number of chromosomes in *Odontophrynus americanus* and *Ceratophrys ornata*.

Odontophrynus americanus has the highest number of chromosomes in an anuran described up to now. *Ceratophrys ornata* is unique among all the amphibians, urodeles and anurans, known up to the present for their high number of chromosomes.

From the cytotaxonomic and evolutionary points of view the taxonomic position of the two genera presents a problem, since they have been considered by Noble[4] as belonging to the family Bufonidae and by Davies[5] to the family Leptodactylidae, the karyotype of which is characterized by a diploid number of $2n = 22$ chromosomes. We suggest that the genera *Odontophrynus* and *Ceratophrys* should be included in a different group, as they appear in the amphibian list published by Cei[6] but forming part of the family Ceratophrydae.

In all the species described here, the chromosomes of the first meiotic metaphase were found to be highly condensed, with two distal localized chiasmata. The primitive annular configuration exhibited by the bivalents during the diplonema remains masked at the moment of the metaphase. None of the species studied shows sex chromosomes that could be differentiated by cytogenetical analysis.

Our observations thus support the views of Galgano[7], Saez *et al.*[8] and Wickbom[9], with reference to the problem of the existence of sex chromosomes in the amphibians.

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ANTHROPOLOGY

The Kanam Jaw

SINCE Dr. and Mrs. L. S. B. Leakey discovered that the Oldowan pebble tool-maker in Tanganyika was an Australopithecine (*Zinjanthropus boisei*)[1], I have been frequently asked whether this development has any bearing on the unsolved problem of the Kanam mandible which was recovered by Dr. Leakey in 1932 from deposits in Kenya apparently at the same cultural horizon as the newly discovered Olduvai skull. The Kanam mandible was referred to *Homo kanamensis* sp. nov.[2] and is preserved in the British Museum (Natural History).

As the Kanam mandible has small front teeth and an apparent chin it was regarded by some authorities as indicating the existence of the modern type of man in Lower Pleistocene times, but Prof. P. G. H. Boswell, having formed the opinion in the field that the geological age of the specimen was not beyond doubt, suggested that it should be placed in "a suspense account" pending further discoveries[3].

Attempts have been made during recent years to establish whether the Kanam mandible was or was not contemporaneous with Lower Pleistocene fauna at the site of discovery; but in summary the results were ambivalent. In volcanic soils, particularly under tropical conditions, the chemical dating methods are admittedly unreliable. In 1952 I pointed out that the fluorine/phosphate ratio of the Kanam mandible was higher than that of any fossil bone that had been tested[4]; yet in 1958 radiometric assays (for adsorbed uranium) gave results which led me to write "our doubts about its antiquity have been re-inforced"[5]. But those doubts were primarily morphological in basis.

Prof. P. V. Tobias, of the University of the Witwatersrand, has recently re-investigated the morphology of this mandible with particular reference to the apparent chin or mental eminence (see following communication). Meanwhile, I wish to direct attention to a fact which may have escaped notice. Sir Arthur Keith in 1948 had come to the conclusion that the Kanam mandible was probably Australopithecine. This is what he wrote: "Dr. Leakey believed, and I agree[d] with him, that the Kanam mandible was evidence of the early development of the modern type of man. Both he and I were then ignorant of the fact that small incisors and canines were also characteristic of the South African Dartian anthropoids [Sir Arthur Keith's name for Australopithecines]. It seems to me now to be much more probable that the small front teeth of Kanam man indicate a relationship to Dartian anthropoids rather than to any type of modern man"[6].

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The controversial mandibular fragment from Kanam in Kenya Colony has long been placed in a 'suspense account' by most palæo-anthropologists. There is little doubt that the presence of an ostensibly well-developed chin in this fossil, for which a Lower Pleistocene age was claimed[1], proved a difficult pill to swallow. As long as the over-simplified notion prevailed that a chin signified *Homo sapiens* and, as long as the Kanam fragment was deemed to possess a chin, one had to explain the unexpected presence of *Homo sapiens* in a Lower Pleistocene deposit or discard either the dating of the deposit or the association of the jaw with the deposit.

In 1955, I was granted permission to re-examine the jaw fragment by the British Museum (Natural History) and, in particular, by Dr. K. P. Oakley and by Dr. L. S. B. Leakey. On first examining the specimen I was struck by two previously unreported facts: first, the 'chin' was represented by an asymmetrical fullness situated largely to the left of the symphyseal surface which had earlier been diagnosed as a "sub-periosteal ossifying sarcoma"[2]. The possibility that the 'chin' was in reality largely a bony reaction to the pathological lesion was heightened by the second observation, namely, that of the elements comprising the mental trigone normally sculptured on the front of a chin, the mental tubercles were completely absent and the mental protuberance was extremely poorly developed. Clearly a detailed morphological re-analysis was essential, and the results of such a study were presented by me at the fourth Pan-African Congress on Prehistory in August 1959[3]. The detailed account will appear in the Proceedings of that Congress.

As a result of the study, I have reached the conclusion that the chin of Kanam man has been greatly over-estimated. In fact, I am convinced that the Kanam fossil does not represent a sapient type of man, but rather belongs to a group of fossils from Africa, known variously as 'palæoanthropic', 'neandertaloid' or 'rhodesioid'. None of the characteristics originally used to define the structure of *Homo kanamensis* (to which the specimen was earlier assigned)[4] is morphologically valid, and the species designation must therefore lapse. On the other hand, a different series of primitive features has impressed me in the re-study. These are:

(1) The great depth in the symphyseal region (40·5 mm. as measured, at least 42·0 mm. as estimated), aligning Kanam with such primitive forms as *Pithecanthropus*, *Atlanthropus*, Mauer and Wadjak, as well as with Cro-Magnon man and several fossils from South and East Africa.

(2) The tremendous depth in the region of M_1 (at least 40·0 mm.), in which respect Kanam exceeds all other mandibles with which it was possible to compare it.

(3) The lack of tapering in body-height between symphyseal and molar regions, which likens the Kanam jaw to those of *Sinanthropus* and *Atlanthropus*, including Sidi Abderrahman.

(4) The very great thickness in the region of M_1 (16·5 mm.), in which feature Kanam is exceeded only by Ternifine I, Heidelberg and Sidi Abderrahman, while it is more or less equal to Ternifine II, *Sinanthropus G.*I., Rabat, Dire-Dawa, Cave of Hearths and La Chapelle.

(5) The rudimentary character of the two elements of the chin present, namely the mentum osseum and the mental protuberance, as in the mandibles of La Quina, La Ferrassie, Spy and Rabat.

(6) The presence of a planum alveolare and of a genial fossa and inferior transverse torus, as in Rabat and Dire-Dawa.

(7) The combination of very small incisors and rather large canines, a likeness with some of the Australopithecinae to which Keith directed attention in 1948, as pointed out by myself at the fourth Pan-African Congress on Prehistory in August 1959 and by Dr. K. P. Oakley (see previous communication).

Several, though not all, of these features might be encountered individually as exceptional variants among modern African mandibles. However, the ensemble of features in a single mandible tends to exclude the Kanam jaw from the *Homo sapiens* group and to relate it rather to a group of earlier African fossil men. Its morphological features align it most closely with the Upper Pleistocene mandible from Dire-Dawa, in the Harrar District of Abyssinia[5], and the Middle Pleistocene Rabat fragment from the

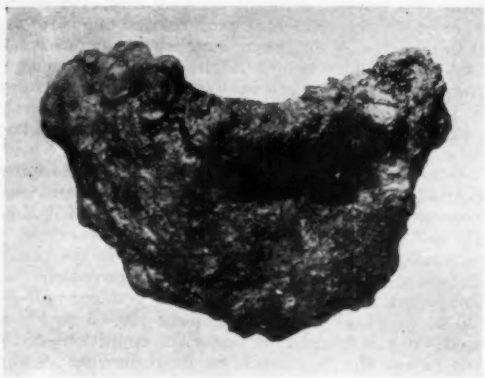

Fig. 1. The Kanam mandible. The fullness of the so-called chin is seen on the right, clearly demarcated by a highlight. The sockets and roots of the missing teeth are apparent; the surviving two right premolar teeth can be seen

Atlantic seaboard of Morocco[6]. On the other hand, the Ternifine mandibles of *Atlanthropus* show more archaic features than do those of Kanam, Rabat and Dire-Dawa; while the Kanam mandible has several morphological features comparable with those of Sidi Abderrahman, though the crucial evidence of the chin region and the retro-symphyseal surface is lacking[7]. As to the possibility of australopithecine affinities, the main resemblance is in the size proportions of the front and back teeth. A few ape-man specimens have, in addition, a degree of chin development faintly reminiscent of that of Kanam.

Thus, while we cannot entirely exclude the possibility that the Kanam jaw is related to a member of the Australopithecinae or of *Atlanthropus*, the balance of evidence supports the view that the Kanam mandible represents a third African fossil showing a cluster of features morphologically intermediate between those of *Atlanthropus* and those of modern man. Whether or not it is justifiable to describe these forms as neandertaloid, thereby relating them by implication to European forms, is a problem which must await more material and further analysis.

At least, it is no longer necessary or correct to build theories upon the alleged 'sapient' or 'modern' morphology of Kanam man; nor should the specimen be interpreted as providing evidence in favour of the

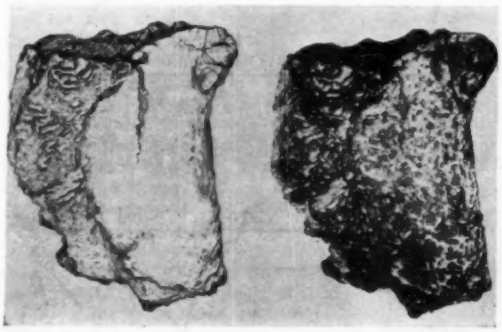

Fig. 2. Sketch and photograph of a section through the Kanam mandible, to show the large pathological mass on the retrosymphyseal surface. The section has passed through the right first incisor root

presapiens theory espoused by Vallois[8]. Perhaps most importantly of all, we are now in a position to consider the age of the Kanam specimen, free from any misconceptions that it is of sapient character.

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Fossilized Human Remains from Northern Kenya

DURING the summer of 1959, a party from the Durham Colleges visited the remote district of Turkana in northern Kenya to carry out a geological survey of the Lothidok and the Labur ranges of hills, which border the western shore of Lake Rudolf.

The rocks which compose the Lothidok range are probably Miocene; but a thick sequence of younger lacustrine sediments is developed against the eastern flank of the Lothidok range, immediately south of the Kalalokoil River (approximate position 35° 47′ E., 3° 26′ N.). C. Arambourg[1] has stated that their age is Upper Pleistocene. These lacustrine beds represent deposition in an ancient Lake Rudolf of far greater extent than the existing lake, since they stand between two hundred and three hundred feet above present lake-level. In places, the Miocene lavas and agglomerates of the Lothidok range must have formed a rocky shore-line to this ancient lake, during a part of Pleistocene times. From the western marginal facies of the lake beds, adjacent to their contact with the Miocene, the Durham Colleges party recovered portions of two fossilized human skulls which are the first remains of this kind to be found in the northern region of Kenya. One is represented by little more than the frontal bones and the upper margins of the orbits. The other skull, with which this communication is chiefly concerned, lacks only the face and the left side of the jaws. A few cervical vertebræ and ribs, and part of a humerus were intimately associated with the second skull.

The more complete skull has been slightly distorted during its enclosure in the lake sediments, but it is possible, without further preparation, to distinguish certain salient features of the skull. The cranial bones, which, incidentally, are fully lithified, are unusually thick (12 mm. or more). The skull is long and conspicuously narrow, although the latter character is exaggerated by crushing; and the face appears to have been small. There is no more than a suggestion of a supra-orbital torus, but the brow is remarkably low. The lower jaw (Fig. 1) is very robustly constructed, with a deep horizontal ramus 22 mm. thick below the third molar; and the mandible seems to have possessed a chin. The molar teeth are very badly worn, being planed down almost to the level of the inferior margin of the enamel. They

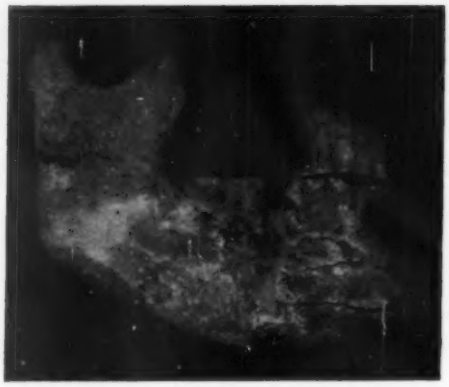

Fig. 1. Lateral aspect of the right branch of a fossilized human mandible, together with a fragment of the upper jaw; from Turkana, northern Kenya (half natural size)

are probably a trifle larger than is the average in Recent individuals of *Homo sapiens*.

Numerous artefacts were found afterwards on sites adjacent to this fossilized human skull, but all were surface finds. None was found *in situ*. The implements include Middle Sangoan hand-axes and Levallois-type flake tools fashioned in chert, small stone points of Solutrean aspect, and barbed harpoon heads and spatulæ of bone. Neighbouring sites also yielded rather poorly preserved remains of various fossilized mammals, including hippos, antelopes and pigs, as yet not properly identified.

It is too early to speculate upon the nature or status of the skull, but there seem to be some clear physical resemblances to the most complete of the Kanjera skulls, which were recovered by L. S. B. Leakey nearly thirty years ago from Pleistocene lake beds developed on the flank of Homa Mountain in western Kenya. Dr. Leakey has suggested a Middle Pleistocene date for the Kanjera skulls. So far, it has not been possible to establish with certainty the precise stratigraphical position of the human fossils from Turkana. Attempts to obtain an absolute dating by chemical methods have also proved inconclusive. The uranium content is the same in both the human bones and in fossilized animal bones from neighbouring sites, which are believed to be undoubtedly contemporaneous with the formation of the lake beds, but the actual figure for all this material is abnormally low.

T. Whitworth

Hatfield College,
Durham.

[1] Arambourg, C., *Bull. Mus. Hist. Nat., Paris*, **1**, fasc. 1 (1935).

PSYCHOLOGY

Age Differences in Movement Pattern

The literature which describes studies of detailed hand movement patterns contains few references to changes in acceleration during these movements. Such references as do occur are mainly to be found in books on motion study and suggest that a movement occurs in three phases: an acceleration phase to a steady speed, followed by deceleration. For example, Lowry *et al.*[1] give a curve purporting to show this pattern without quoting any evidence to support it. Experimental work carried out here[2] and at Cambridge by Singleton[3] suggested that movement patterns of older people might differ from those of young and, since no relevant evidence could be found in the literature, an ultra high-speed chrono-cyclographic technique was developed in order to make a detailed study of movement patterns.

Our subjects were required to make simple movements in response to a four-choice stimulus and these were photographed with a light on the hand flashing at 100 flashes per second. Three conditions of response were used which differed only in the manipulation demanded after the initial movement was completed. Matched groups of 12 younger subjects (20–25 yr.) and 12 older subjects (60–65 yr.) were used. It was found that under the conditions of this experiment the movement, far from showing a simple acceleration : constant speed : deceleration pattern, showed marked variations in acceleration throughout. Typically, instead of the smooth acceleration which might have been expected, the movement pattern showed very rapid acceleration at the outset, followed by an equally rapid decrease in acceleration to a minimum at approximately 0·1 sec. from the commencement of the movement, which was in turn followed by a second acceleration to a 'peak' of approximately half the value of the first. This whole phase occupied approximately a third of the total movement time. While the characteristic pattern at the outset of the movement was found in both young and old subjects, the old subjects accelerated less rapidly than the young and the 'dip' passed below the zero acceleration line showing that the older men had a short negative acceleration phase. Fig. 1 shows a typical velocity curve for an older subject with the acceleration curve derived from it. There were, within the young and old groups, no statistically significant differences between the three response conditions tested, but between groups there were significant differences in response initiation time in

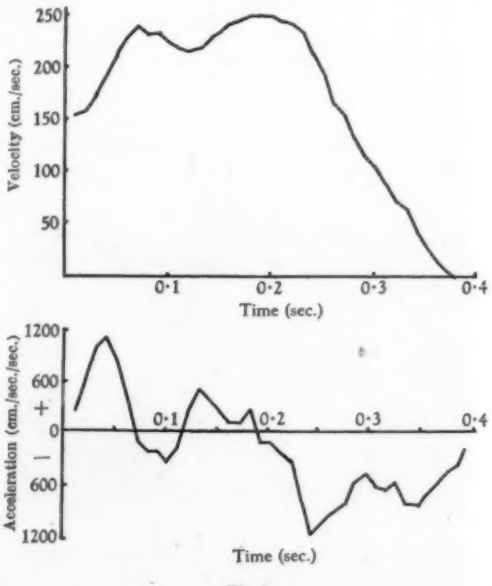

Fig. 1

two of the conditions. Movement times were not significantly different. The magnitude of the initial acceleration and the depth of the 'dip' were significantly different between young and old.

This typical pattern does not appear to occur when a 'free' movement is made in the subject's own time and no stimulus is given or specific response demanded. This suggests that the 'dip' in the initial phase of a 'controlled' movement is in some way associated with either the presence of the visual stimulus or the need to make a response, or both. 'Free' movement patterns do, however, show cyclic periods of acceleration, which are also to be found in the latter two-thirds of the 'controlled' movements. There is a possibility that these may be similar to the oscillations of a particular frequency which have been reported in muscular tremor and static pressure by a number of workers (for example, Hammond *et al.*[4]). If this is so then it would appear that this periodicity will occur in 'free' movements as well as in the static condition.

These results suggest several theoretical possibilities, but the techniques used in this pilot experiment were not sufficiently precise for us to obtain all the information we would need to establish a theoretical model. Work is therefore proceeding with further refined techniques.

K. F. H. Murrell
D. G. Entwisle

Department of Psychology,
University of Bristol.

[1] Lowry, S. M., Maynard, H. B., and Stegemerten, G. J., "Time and Motion Study", 129 (McGraw-Hill, New York, 1940).
[2] Griew, S., *Amer. J. Psychol.*, **72**, 83 (1959).
[3] Singleton, W. T., *Brit. J. Psychol.*, **14**, 166 (1954).
[4] Hammond, P. H., Merton, P. A., and Sutton, G. G., *Brit. Med. Bull.*, **12**, 214 (1956).

Experimental Evidence for Extra-Sensory Perception

In his communication in *Nature* of November 7, p. 1515, Mr. C. E. M. Hansel cites certain results from the Shackleton experiments in precognitive telepathy which he claims support his theory that the guessers made 'card substitutions' on prearranged positions on the scoring sheets. In a forthcoming paper in the *Proceedings of the Society for Psychical Research*, I have shown on quite other grounds how extremely improbable it is that such a method was used. I cannot accept Mr. Hansel's arguments based on the 1,139 (+ 2) trials carried out at rapid rate, because, as I shall show, he makes an unwarranted assumption.

What Mr. Hansel has brought to light in his communication is a most interesting 'segmental salience' effect which had previously escaped notice. Card guessers, as a rule, naturally think of a run of 25 trials as being broken up into five successive groups or 'segments' each of five trials. Most scoring sheets have a thick line, drawn after trials 5, 10, 15, 20 and 25. Subconsciously, many guessers tend to envisage their work as a succession of smaller tasks or separate experiments, each consisting of five trials. Now ever since the year 1941, Prof. J. B. Rhine and his colleagues at Duke University have observed that many percipients tend to distribute their 'hits' according to more or less regular patterns throughout the five guesses of a segment, or in the five segments of a run of 25. Three main types of 'salience' have been distinguished: (*a*) 'terminal' salience in which, in the composite pattern of a segment, the first and last trials score above chance expectation while the three middle trials give a score at about 'chance' level or below it; (*b*) 'middle' salience in which the two end trials give scores at, or below, chance expectation and the three middle trials score above 'chance' level; (*c*) 'decline' salience in which, say, the first three trials are well above 'chance' expectation, after which a decline sets in and the score falls to 'chance' level through the last two trials. Similar 'salience' patterns may occur either in the pooled scores of the five trials of the segment or in the five segments of the run, or 'segment' and 'run' salience may occur together, in which case there is sometimes a high degree of positive correlation between them.

These same patterns have been observed during thousands of trials, as, for example, in the long-distance experiments of Dr. Marchesi[1] in which 'middle' salience occurred both in the segment and run over a series of 8,825 trials. It has been noted in 'precognitive' as well as in 'direct' target-guessing.

The Shackleton (+ 2) *trials*. In order to clarify the issue, I shall neglect the 144 trials which occur in positions Nos. 21, 22, 23 of the scoring sheet of 23 (+ 2) trials, since these do not form complete segments. This leaves us with a total of 995 (+ 2) trials in places Nos. 1–20. On these there are 297 (+ 2) hits which are pooled and distributed over the five successive positions in the segment as in Table 1.

Table 1

Position	Trials	Hits	Deviation*	'Odds' against chance
I	199	61	$4{\cdot}2 \times$ S.D.*	$> 1{\cdot}6 \times 10^4$ to 1
II	200	72	$5{\cdot}6 \times$ S.D.	$> 2{\cdot}6 \times 10^7$ to 1
III	200	70	$5{\cdot}3 \times$ S.D.	$> 1{\cdot}7 \times 10^6$ to 1
IV	198	51	$2{\cdot}0 \times$ S.D.	20 to 1
V	198	43	$0{\cdot}6 \times$ S.D.	—
Totals	995	297	—	—

* S.D., standard deviation $= 0{\cdot}4\sqrt{n}$, where n is number of trials Expected score, $n/5$.

It is seen that the scoring-rate reaches a peak at Trials II and III, and afterwards declines to the chance-level. It would appear that at the 'rapid' rate of calling, the extra-sensory perception effect is temporarily exhausted after the third trial, and recovers at the start of the next segment (see Fig. 1). On the first three trials there is a total of 203 hits in 599 (+ 2) trials, as compared with a total of 94 hits in 396 (+ 2) trials. The 'salience' in the segment is mainly of type (*C*), and represents a kind of 'position' effect.

So common were these 'salience' effects in the 'segment' or the 'run' that in 1941 Dr. J. A. Greenwood[2] developed a most elaborate statistical method for evaluating 'salience ratios' and they were even employed as a means of detecting the presence of extra-sensory perception in cases where the deviations from chance expectation in an experiment were not in themselves significant[3]. The assumption is that in certain cases extra-sensory perception produces both positive and negative deviations which may cancel each other out in the long run.

By using Fisher's method for evaluating the significance in the difference of the means of two small samples, I find that the odds against the hypothesis that the difference in the scoring-rates of the two groups (I, II, III) and (IV, V) is due to

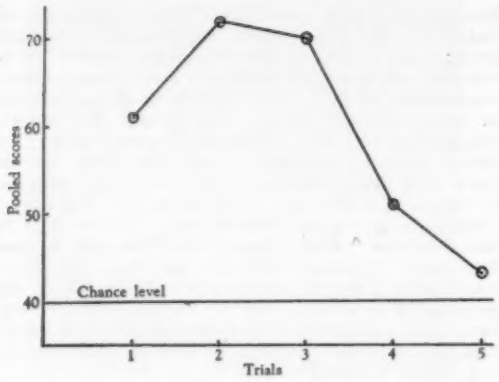

Fig. 1. Score pattern in segment

chance certainly far exceed 1,000 to 1 and are probably of the order of 10^4 to 1, as checked by a different method. The five segments of the run considered as five different units, however, exhibit no evidence of salience; that is, there is not a decline effect in the run itself.

Now the fundamental 'null' hypothesis on which Mr. Hansel has based his expectations of hits and misses in the five trials of the segment is the assumption that, even when extra-sensory perception is functioning at a high level, there ought to be approximately equal numbers of hits (or successes) on equal numbers of trials selected from different pre-assigned positions on the scoring-sheet. But the numerous 'decline' effects observed in both the run and the segment by American investigators show that this assumption is not justified. Further, it has been the experience of Mr. G. N. M. Tyrrell and others that with high scoring subjects such as Miss Johnson, the 'hits' often crowd themselves into unbroken runs of as many as 7 or 8 or more in a run. That is, extra-sensory perception does not function continuously but in spurts. In other words, given a fixed number of hits, these are often found not to be randomly distributed over the 25 cells of the scoring-sheet, but to favour certain positions in the segment or run or in relation to one another.

The 'periodic' effect cited by Mr. Hansel is the result of the 'salience' pattern and constitutes evidence that such a pattern exists that is, on the average, repeated from segment to segment. Similarly, the high scores on the mid-segment trial are simply due to the fact that the peak of the salience happens to coincide with the mid-segment trial and the one preceding.

If an extra-sensory perception salience effect exists, it follows that there may be significantly differing numbers of hits on the different trials of the segment.

Once the existence of extra-sensory perception (the origin of which is utterly mysterious) is admitted, it may be expected to produce many other secondary effects that are surely not more surprising than the existence of the faculty itself.

For, whatever this power may ultimately prove to be, it certainly seems to have some attributes of human intelligence and is not merely a random physical process. It may well be that the subjects who possess this mysterious means of acquiring information have also subconscious personal predilections for certain types of effect, and can at times produce them by unconscious motivation. Thus, we know that one of Prof. Rhines's major subjects could at will orient his mind so as to produce below-chance scores instead of his usual high scores.

S. G. Soal

28 Thurleigh Road,
London, S.W.12.

[1] *J. Parapsychol.*, **6**, 52 (1942).
[2] Greenwood, J. A., *J. Parapsychol.*, **5**, 245 (1941).
[3] Rhine, J. B., *J. Parapsychol.*, **5**, 183 (1941).

Dr. Soal agrees that there is a periodicity in the 'guessers' scores which are related to the line numbers on the score sheet. He calls this effect 'salience' and I will also use this nomenclature. It must, however, be understood that by 'salience' we mean this periodicity in the scores without advancing any theory as to its cause.

Dr. Soal and I agree on the fact that Shackleton consistently produced scores which cannot be attributed to chance. Dr. Soal attributes these scores to telepathy. He regards salience effects as secondary characteristics of telepathy and to explain them he introduces subsidiary hypotheses which can be summarized as follows: (1) Certain guessers 'subconsciously' divide the sequence of twenty-five trials into five 'tasks' of five trials each. Other guessers think of the whole twenty-five trials as the 'task'. (2) At some point in the task, whichever type it be, either towards the end of it, or in the middle of it, or at the two ends of it and not in the middle, some guessers lose their telepathic abilities and their scores fall to the chance-level. (3) In the case of other guessers, they do not lose their telepathic abilities at these positions in the task, but they are "unconsciously motivated" to avoid securing hits and their scores fall below the chance-level.

I have shown that the results of the Soal–Goldney experiment could have been produced by means of a trick which involved memorizing a code. The particular salience effect produced by Shackleton would inevitably arise if such a trick was used, although its presence in the grouped data could be masked if the operators changed their code in a systematic manner.

It is not surprising that salience effects have been observed in other experiments on extra-sensory perception; for they may arise if there are factors which are not adequately controlled in the experimental conditions, or if a trick is being employed. It should further be noted that both errors due to poor experimental design, and confessed trickery, are not uncommon in psychical research, whereas precognition and telepathy are hypothetical processes.

In the case of the Shackleton experiments the issue is quite clear. The scores produced by Shackleton could be obtained by using a trick. Such a trick would, possibly, but not necessarily, reveal itself by causing a periodicity to arise in the scores. Such a periodicity is present in the results of the 'rapid-rate' experiments. It cannot be explained away by calling it 'salience', for this is merely another name for the observed periodicity. To explain salience effects in terms of telepathy, Dr. Soal has produced a number of subsidiary hypotheses which I regard as being as unlikely as is the existence of precognitive-telepathy itself.

C. E. M. Hansel

Department of Psychology,
University of Manchester.

FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, March 28

ROYAL GEOGRAPHICAL SOCIETY (at 1 Kensington Gore, London, S.W.7), at 5 p.m.—Miss A. Coleman and Mr. K. R. A. Maggs: "A New Land Use Survey".

RADAR AND ELECTRONICS ASSOCIATION (at the Royal Society of Arts, John Adam Street, Adelphi, London, W.C.2), at 7.30 p.m.—Mr. Peter D. Hall: "Computers—Some Design Problems of Large Scale Computers".*

Tuesday, March 29

INSTITUTION OF ELECTRICAL ENGINEERS, EDUCATION DISCUSSION CIRCLE (at Savoy Place, London, W.C.2) at 6 p.m.—Discussion on "The Place of Illumination in Electrical Engineering", opened by Mr. G. F. Freeman.

INSTITUTION OF MECHANICAL ENGINEERS, EDUCATION GROUP (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Discussion on "The Need for Post-Graduate Refresher Courses for Engineers in Industry".

SOCIETY OF INSTRUMENT TECHNOLOGY (at Manson House, 26 Portland Place, London, W.1), at 7 p.m.—Mr. G. G. Bloodworth: "Application of Transistors in Instrumentation".

Tuesday, March 29—Thursday, March 31

INSTITUTE OF METALS (at Church House, Great Smith Street, Westminster, London, S.W.1)—Spring Meeting.

Tuesday, March 29

At 11 a.m.—Sir Ronald Prain, O.B.E.: "Mineral Resources and Metal Reserves" (Presidential Address).

At 6.30 p.m.—Prof. P. M. S. Blackett, F.R.S.: "The Magnetism of Rocks and Continental Drift" (May Lecture).

Wednesday, March 30

INSTITUTE OF METALS, METAL PHYSICS COMMITTEE (in the Hoare Memorial Hall, Church House, Great Smith Street, Westminster, London, S.W.1), at 2.30 p.m.—Meeting on "New Aspects of the Electron Theory of Metals".

OIL AND COLOUR CHEMISTS' ASSOCIATION, LONDON SECTION (at he Royal Society of Tropical Medicine and Hygiene, Manson House, 26 Portland Place, London, W.1), at 7 p.m.—Dr. H. B. Footner: "Painting in the Petroleum Industry".

Wednesday, March 30—Thursday, March 31

PLASTICS INSTITUTE (at the University of London, London, W.C.1)—Conference on "Polymeric Progress".

Thursday, March 31

INSTITUTE OF METALS (at Convocation Hall, Church House, Great Smith Street, London, S.W.1), at 10 a.m.—Discussion on "Vacancies, Ageing and Precipitation".

ROYAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Dr. N. F. Astbury: "Science in the Ceramic Industry".

MINERALOGICAL SOCIETY (at the Geological Society of London, Burlington House, Piccadilly, London, W.1), at 5 p.m.—Scientific Papers.

UNIVERSITY OF LONDON INSTITUTE OF EDUCATION (in the Great Hall, Goldsmiths' College, New Cross, London, S.E.14), at 5 p.m.—Sir Edward Boyle, Bt., M.P.: "Education—Tradition and Change".*

INSTITUTION OF ELECTRICAL ENGINEERS (at Savoy Place, London, W.C.2), at 5.30 p.m.—Prof. C. F. Powell, F.R.S.: "Cosmic Radiation" (Fifty-first Kelvin Lecture).

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

LECTURER (male) IN CHEMISTRY—The Principal, Borough Road College, Isleworth, Middlesex (March 31).

LECTURER (Physical Chemist, with postgraduate research experience, and preferably a higher degree and experience in electronics) IN THE DEPARTMENT OF ELECTRICAL ENGINEERING—Prof. A. Tustin, Department of Electrical Engineering, Imperial College of Science and Technology, London, S.W.7 (March 31).

LECTURER (with a specialized knowledge in at least one of the following fields and prepared to undertake or supervise research: metallurgical analysis, refractories, nonferrous extraction, physical metallurgy) IN METALLURGY—The Registrar, The Manchester College of Science and Technology, Manchester 1 (April 2).

RESEARCH OFFICER (graduate, with an honours degree in geography, and planning experience) IN THE COUNTY PLANNING DEPARTMENT—The Establishment Officer, Shire Hall, Bedford (April 2).

BIOCHEMIST (M.Sc. or Ph.D. in biochemistry or physiological hemistry, and at least three years experience in the procedures of biochemistry or chemical pathology) with the Limerick County Council, Ireland—The Secretary, Local Appointments Commission, 45 Upper O'Connell Street, Dublin (April 5).

SENIOR TECHNICIAN (skilled cartographer) IN THE DEPARTMENT OF GEOGRAPHY—The Registrar (G8T), Queen Mary College (University of London), Mile End Road, London, E.1 (April 8).

LECTURER (medically or non-medically qualified) IN BIOCHEMISTRY; an ASSISTANT (medically or non-medically qualified) IN PHYSIOLOGY; and an ASSISTANT (preferably applied mathematician) IN MATHEMATICS—Joint Clerk to the University Court, Queen's College (University of St. Andrews), Dundee (April 9).

LECTURER (with qualifications and a special interest in the teaching of chemistry) IN EDUCATION—The Registrar, The University, Sheffield (April 9).

ASSISTANT LECTURER or LECTURER (with a special interest in the philosophy of science) IN PHILOSOPHY—The Registrar, The University, Hull (April 12).

DEPARTMENTAL ASSISTANT IN ANIMAL PHYSIOLOGY at the School of Agriculture, Sutton Bonington, near Loughborough, for demonstration and laboratory work in animal physiology, with opportunities for research—The Registrar, The University, Nottingham (April 12).

LECTURER (with special qualifications in engineering geology, including hydrology and soil science) IN THE DEPARTMENT OF GEOLOGY, University of the Witwatersrand, Johannesburg, South Africa—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (South Africa and London, April 15).

ASSISTANT PROFESSOR OF PHYSICAL CHEMISTRY in the Faculty of Arts and Science, Memorial University of Newfoundland, Canada—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Canada and London, April 15).

UNIVERSITY LECTURER IN STATISTICS—The Secretary of the Appointments Committee of the Faculty of Mathematics, the Arts School, Bene't Street, Cambridge (April 18).

CHAIR OF SOIL SCIENCE in the Faculty of Agriculture, University of Khartoum—The Registrar, University of Khartoum, c/o Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (April 20).

ASSISTANT LECTURERS or LECTURERS (2) (with a good honours degree in geology) IN THE DEPARTMENT OF GEOLOGY—The Registrar, University College of North Staffordshire, Keele, Staffs (April 23).

LECTURER IN THE DEPARTMENT OF GEOGRAPHY, University of the Witwatersrand, Johannesburg, South Africa—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (South Africa and London, April 25).

LECTURER or ASSISTANT LECTURER (man or woman graduate with a special interest in petrology) IN GEOLOGY—The Secretary, Bedford College (University of London), Regent's Park, London, N.W.1 (April 25).

ASSISTANT LECTURER IN PHYSIOLOGY at the University of Hong Kong—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Hong Kong and London, April 29).

LECTURER IN CHEMICAL ENGINEERING—The Registrar, University College, Singleton Park, Swansea (April 30).

POST-DOCTORAL RESEARCH FELLOW IN THE DEPARTMENT OF ORGANIC CHEMISTRY, to work in collaboration with Dr. A. R. Battersby on the chemistry of natural products, particularly in the alkaloid field—The Registrar, The University, Bristol (April 30).

SCIENTIFIC OFFICERS/SENIOR SCIENTIFIC OFFICERS (with a first- or second-class honours degree, previous research experience in some experimental branch of physics, chemistry or engineering, and at least three years postgraduate experience for Senior Scientific Officer) IN THE BASIC PHYSICS DIVISION, National Physical Laboratory, Teddington, Middlesex, to do fundamental research on physical and chemical properties of solids at very high pressures—The Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting A.119.OA (April 30).

SENIOR LECTURER IN PHYSICAL CHEMISTRY at the University of Natal, Pietermaritzburg, South Africa—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (South Africa and London, April 30).

DEMONSTRATOR IN PHYSICAL CHEMISTRY—Head of the Physical Chemistry Laboratory, The University, South Parks Road, Oxford (May 15).

CHIEF OF THE DIVISION OF LAND RESEARCH AND REGIONAL SURVEY, Commonwealth Scientific and Industrial Research Organization, Canberra, A.C.T., Australia—Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2, quoting Appointment No. 570/84 (May 21).

POST-DOCTORAL FELLOWS (2) IN THE CHEMISTRY DEPARTMENT, for work on (*a*) electrode processes and (*b*) thermodynamics of polymer solutions—Prof. B. E. Conway, Department of Chemistry, University of Ottawa, Ottawa, Canada (May 21).

ASSISTANT EDITOR (man or woman graduate with some knowledge of chemistry, and preferably sub-editing experience with scientific publishers) for the less academic aspects of scientific publications—The General Secretary, The Chemical Society, Burlington House, Piccadilly, London, W.1.

ASSISTANT EXPERIMENTAL OFFICER (with at least G.C.E., Scottish Leaving Certificate, Higher National Certificate, or equivalent, and some experience of histological techniques), to undertake histological work and to assist in the Pathology Department—The Secretary, Rowett Research Institute, Bucksburn, Aberdeen.

ASSISTANT, Grade B (with a good honours degree, and preferably industrial or research experience), for mathematics—The Clerk to the Governors, South-East Essex Technical College, Longbridge Road, Dagenham, Essex.

ASSISTANT PROFESSOR TO TEACH METALLURGICAL THERMODYNAMICS AND KINETICS—Head, Department of Metallurgy, Montana School of Mines, Butte, Montana.

DEMONSTRATOR IN BIOLOGY within the Department of Botany and Zoology—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1, or the Registrar, University of Adelaide, Adelaide, Australia.

EXPERIMENTAL PHYSICISTS (with at least a good second-class honours degree and preferably postgraduate experience in some aspect of nuclear physics), to (*a*) collaborate with physicists designing a 7-GeV. proton synchrotron, and take responsibility for aspects of selection, analysis and transport of high energy beams and eventually

to participate in high energy nuclear research; and (*b*) to work with nuclear physicists using a 50-MeV. linear accelerator and collaborate with university physicists using this machine—The Secretary, Rutherford High Energy Laboratory, Harwell, Didcot, Berkshire, quoting Ref. 1637/34.

MASTER (with high academic qualifications) TO TEACH MATHEMATICS to open scholarship standard; and a MASTER TO TEACH PHYSICS AND/OR CHEMISTRY to A level—The Headmaster, Blundell's School, Tiverton, Devon.

PHYSICIST (with a degree or equivalent in general science including physics, or in chemistry with physics subsidiary, experience in handling radioactive materials and health physics, and preferably a knowledge of electronics and/or general explosive practice) at the Ministry of Aviation H.Q., London, to be responsible for developing effective production methods for radioactive and allied materials and supervision of safety methods allied to health physics at the factory—The Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting Ref. A.118/O.A.

PRINCIPAL GRADE PHYSICIST (with experience either in hospital physics or in some relevant field, such as biophysics, electronics or nuclear physics), to initiate work on physics applied to the various fields of medicine (other than radiotherapy)—The House Governor, The Queen Elizabeth Hospital, Edgbaston, Birmingham 15.

SENIOR LABORATORY TECHNICIAN, to be responsible for new physics teaching laboratories and lecture demonstrations up to degree standard—The Secretary, King's College, Strand, London, W.C.2, quoting Ref. 3066.

SENIOR TECHNICIAN II (with some organizing ability, and preferably previous experience in medical or biological research) IN THE CANCER RESEARCH LABORATORY, for work in connexion with the cytology and cytochemistry of human tumours—The Administrative Officer, Mount Vernon Hospital, Northwood, Middx.

SOIL CHEMIST (with an honours degree in chemistry, or in natural science including chemistry, and at least two years postgraduate training or experience as a soil chemist) at the West African Institute for Oil Palm Research, Nigeria, for the study and analysis of soil types with a view to improving soil conditions—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.197/199/016/T.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

British Steel Castings Research Association. British and Foreign Specifications for Steel Castings, Part 1—Summaries, Comparisons and other relevant Information. Pp. xiv+48. (Sheffield: British Steel Castings Research Association, 1959.) 40*s.*; 7.50 dollars. [121

Society for Freedom in Science. Occasional Pamphlet No. 19 (December, 1959): Opposition Aroused in China by Marxist Planning of Scientific Research. Pp. ii+16. (Oxford: Dr. John R. Baker, Dept. of Zoology, University Museum, 1959.) [121

Ministry of Agriculture, Fisheries and Food. Fishery Investigations, Series II, Vol. XXII, No. 8: The Spawning of the Plaice (*Pleuronectes platessa*) in the Irish Sea. By A. C. Simpson. Pp. ii+30. (London: H.M. Stationery Office, 1959.) 9*s.* net. [121

University Scholarships for Student Apprentices in Electrical, Electronic and Mechanical Engineering. Pp. vii+23 (7 plates). (London: H.M. Postmaster General, 1960.) [121

Institute of Physics. The Teaching of Mathematics to Physicists. Revised Report. Pp. 25. (London: Institute of Physics, 1959.) 2*s.* 6*d.* [121

Ministry of Labour. Factories Acts, 1937 and 1948. Factories—(Ionising Radiations)—Special Regulations—Second Preliminary Draft of Regulations. Pp. 20. (London: H.M. Stationery Office, 1960.) 1*s.* 3*d.* net. [121

Society for the Bibliography of Natural History. Essai sur la Geographie des Plantes (1807). Par Alexander von Humboldt. (Sherborn Fund Facsimile, No. 1). Pp. 38+1 plate. (London: Society for the Bibliography of Natural History, c/o British Museum (Natural History), 1959.) 10*s.* [121

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